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Editorial

Original Articles

Editorial High MMR in Mothers & Children – A major Role of Malnutrition & Micronutrient Deficiencies – NNS 2011

Mohsin Masud Jan
Editor

National Nutrition Survey (NNS) 2011 suggests malnutrition plays a substantial role in Pakistan's high child morbidity and mortality rates

"Well fed people can enhance their dignity, their health and their learning capacity. Putting resources into social programs is not expenditure. It is investment", Luizlnacio Lula da Silva, former President of Brazil.

Finally, the federal government has launched the long-awaited National Nutrition Survey (NNS) 2011 in Islamabad. Findings of the NNS 2011 are depressing and clearly depicts how neglected the subject is in Pakistan. There has been no improvement in nutrition indicators for the last almost four decades and Minister Ahsan Iqbal rightly lamented the fact that the last decade following NNS 2001 has been totally lost as no tangible steps have been taken to improve the situation.

Federal Minister for Planning and Development and the Minister of State for Health Services Regulations and Coordination with the respective secretaries, representatives of the Provincial Governments and the Planning Commission of Pakistan, Donors, UN Agencies and civil society were present at the launching ceremony.

The NNS 2011 was the largest nutrition survey in the history of Pakistan conducted by the Aga Khan University's Division of Women and Child Health, Ministry of Health and UNICEF with the financial support of Aus AID and DFID. The NNS 2011 covered all provinces, Azad Jammu and Kashmir (AJK), Gilgit Baltistan and the Federally Administered Tribal Areas (Fata). This included 1,500 enumeration bocks (EBs)/villages and 30,000 households with a 49 per cent urban and 51 per cent rural distribution.

Results from the NNS 2011 indicated little change over the last decade in terms of core maternal and childhood nutrition indicators.

With regard to micronutrient deficiencies, while iodine status had improved nationally, vitamin A status has had deteriorated and there had been little or no improvement in other indicators linked to micronutrient deficiencies.

The NNS 2011 revealed that the nutritional status has not changed much over the past decade. The anthropometry of children under 5 revealed that 43.7 per cent were stunted (too short for her/his age/low height for age) in 2011 as compared to 41.6 per cent in 2001 NNS. Similarly, 15.1 per cent children were wasted (weight that is too low for her/his height) compared to 14.3 per cent in 2001. As per World Health Organization's standards, a national average of 15 per cent or above is labelled as an "Emergency".

The NNS 2011 indicates that stunting, wasting and micronutrient. deficiencies are endemic in Pakistan. These are caused by a combination of dietary deficiencies; poor maternal and child health; a high burden of morbidity; and low micronutrient content in the soil, especially iodine and zinc. Most of these micronutrients have profound effects on immunity, growth and mental development. They may underline the high burden of morbidity and mortality among women and children in Pakistan.

Malnutrition plays a substantial role in Pakistan's high child morbidity and mortality rates. Due to its correlation with infections, malnutrition in Pakistan currently threatens maternal and child survival and an estimated 35 per cent of all under 5 deaths in the country are linked with malnutrition. It is imperative to respond to the situation if Pakistan has to be on track to achieve Millennium Development Goal (MDG) 4; about two third reduction in under 5 mortality.

More than 1.5 million children in Pakistan are currently suffering from acute malnutrition, making them susceptible to infectious diseases which may even lead to death. Long-term (chronic) malnutrition undermines both physical and mental development; nearly half of Pakistan's children are chronically malnourished, and have their brain development and immune systems impaired, with life-long consequences.

Most of the irreversible damage due to malnutrition happens during conception and in the first 24 months of life meaning that risk begins from the day of conception to up to two years of age also referred to as the first 1000 days.

It was encouraging to listen to the Federal Minister for Planning and Development Ahsan Iqbal, during the launch of the NNS 2011, who was very clear that it is time for retrospection and that the issue is not going to be resolved through routine approach and all the stakeholders should respond to the situation as an emergency.

Besides, the launch of the NNS 2011 another positive development is Pakistan's joining of the Scaling Up Nutrition (SUN) initiative at the global level in April 2013. More than 40 countries have joined the SUN Movement so far, Pakistan being the largest country. The SUN is an opportunity which the government should utilise effectively and gear up to improve the situation of nutrition in the country. Key donors, UN Agencies, National and International NGOs are there to support the federal and provincial governments to scale up efforts for nutrition in a coordinated and efficient manner.

Original Article

HCV

Seroprevalence of Hepatitis C Virus (HCV) in Southern Punjab

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ABSTRACT

Objective: To find out the seroprevalence of Hepatitis C Virus (HCV) detected on blood screening in blood donors and candidates for recruitment in Armed forces of Pakistan from Southern Punjab.

Study Design: Observational study

Place and Duration of Study: This study was carried out in the Department of Pathology, Combined Military Hospital (CMH), Multan from January to December 2013.

Materials and Methods: Serological blood screening of blood donors and candidates coming for recruitment in armed forces of Pakistan at CMH Multan was performed. Test was performed with rapid screening kit initially and suspected cases were confirmed with third generation ELISA technique. Bio-data of Hepatitis C virus (HCV) positive cases was collected, analyzed and compared with national and international literature.

Results: A total of 10666 persons were screened out, 311 (2.91%) were HCV positive.

Conclusion: Seroprevalence of HCV in this region is also high like rest of the world. Public awareness about the disease, blood screening before transfusion, use of disposable syringe, proper disposal of contaminated material and prevention from sexual transmission are required to decrease the incidence and its spread.

Key Words: Hepatitis C (HCV), Blood Screening

INTRODUCTION

Hepatitis C is an infectious disease affecting the liver, caused by the hepatitis C virus (HCV).[1] The infection is usually asymptomatic initially, but chronic infection can lead to scarring of the liver and ultimately to cirrhosis, which is generally apparent after many years. In some cases, those with cirrhosis will go on to develop liver failure, liver cancer or life-threatening esophageal variceal bleeding.[1] HCV is spread mainly by blood transfusion, pricking by infected needle, poorly sterilized medical equipment. An estimated 200 million people worldwide are infected with hepatitis C.[2][3][4] . Hepatitis C initially named as non-A non-B hepatitis in the 1970s and then recognized as separate entity in 1989.[5] Hepatitis C infects human beings and chimpanzees.[6] No vaccine against hepatitis C is available. The virus persists in the liver in about 85% of those infected. This chronic infection can be treated with interferon therapy. Overall, 70% of people treated are cured. [7] Hepatitis C infection causes acute symptoms in 15% of cases.[8] Symptoms are generally mild and vague, including a decreased appetite, fatigue, nausea, muscle or joint pains, and weight loss[9] and rarely does acute liver failure result.[10] Most cases of acute infection are not associated with jaundice.[11] The infection resolves spontaneously in 10–50% of cases [11] About 80% of those exposed to the virus develop a chronic infection.[12] Most of the infected persons remain asymptomatic during initial few decades of infection.[13] Chronic hepatitis C can be associated with fatigue[14] and mild cognitive problems.[15] Late relapses after apparent cure have been reported, but these can be difficult to distinguish from reinfection.[16] Liver cirrhosis may lead to portal hypertension, ascites, easy bruising or bleeding, varices, jaundice, and a syndrome of cognitive impairment known as hepatic encephalopathy.[22] Ascites occurs at some stage in more than half of those who have a chronic infection.[23].

MATERIALS AND METHODS

This is an observational study carried out between January 2013 to December 2013 at Hematology unit, Department of Pathology, Combined Military Hospital (CMH) Multan. All the persons coming for blood screening were included in the study. Majority were the blood donors and others were the candidates for recruitment in Armed Forces of Pakistan appearing at Multan Center from different areas of southern Punjab. Among the Blood donors, majority consisted of volunteers of Armed forces, relative of patients requiring blood at CMH, Departments of Paediatric Surgery, Nishtar Medical College and Hospital and Institute of Child Health, Multan. The study protocol consisted of the informed consent, age, address, occupation, education, marital and socio economic status. Five ml blood was taken from each candidate and screened for various serologically positive infective diseases including Hepatitis C (HCV) by rapid kit screening technique. Seropositivity was confirmed by third generation ELISA technique. All the informations

were collected on a predesigned performa. Results regarding various infective diseases as Hepatitis C, Hepatitis B and HIV were noted. Bio-data of Hepatitis C (HCV) was separated, analyzed and compared with national and international literature.

RESULTS

A total of 10666 persons were screened for Hepatitis C (HCV). Among these, 6216 persons were blood donors and 4450 were candidates for recruitment in Armed forces of Pakistan at Combined Military Hospital (CMH), Multan. In blood donors, 5990 (96%) were males and 226 (4%) were females. All the candidates for recruitment were male. This means that out of 10666 persons, 10440 (98%) were male and 226(2%) were female. Age range was between 18-40 years in blood donors while candidates for recruitment were 18-24 years old. Out of 6216 blood donors, 137(2.20%) were positive. While out of 4450 candidates for recruitments in armed forces of Pakistan 174(3.91%) were positive for HCV. Overall, 10666 persons were screened and 311 (2.91%) were found positive for HCV. Out of 10440 males, 305 (2.91%) and out of 226 females 6(2.65%) were found HCV positive.

Table No.1: Prevalence in Blood Donor Group

Total number Screened	HCV +	Percentage
6216	137	2.20%

Table No.2: Prevalence in Recruits Group

Total number Screened	HCV +	Percentage
4450	174	3.91%

Table No.3: Prevalence as a whole

Gender	Number Screened	HCV +	Percentage
Male	10440	305	2.92%
Female	226	6	2.65%
Total	10666	311	2.91%

DISCUSSION

This study was an attempt to define the seroprevalence of HCV in relatively healthy and young population in Southern Punjab. Data consisted of analysis of the results of blood screening in candidates of recruitment in armed forces of Pakistan and blood donors at CMH, Multan during a year from January to December 2013. The testing method consisted of third generation ELISA technique which is used by the majority of the screening centers. As minimum age limit for blood donation and recruitment in Armed Forces is 18 years, so it was not possible to access the minimum age of acquisition of Hepatitis C in this study. Result of our study showed that prevalence of HCV in blood donors is 2.20%, in candidates for recruitment in armed forces is 3.91% .Overall, prevalence is 2.91%. HCV infection has significant morbidity and mortality worldwide. The global prevalence of HCV is 3%.[24] The World Health Organization has estimated that 200 million people worldwide are infected with HCV[2-4,25]. The prevalence in the USA is estimated in about 1 million people [26]. Khattak et al. reported a 6.2% prevalence of anti-HCV in professional blood donors[27.] Farooq et al. estimated a prevalence of 3.3% for HCV antibodies among young soldiers[28]. Butt et al reported the prevalence of HCV 1.70%. Similar results have been reported by Zakaria et al. with a 2.2% prevalence of HCV antibodies among recruits of Pakistan armed forces[29].

CONCLUSION

In this study, prevalence of HCV is comparatively high. Certain steps should be taken to stop the increasing trend of Hepatitis C like monitoring disease incidence and determine the sources of infection and modes of transmission. Certain control measures should be taken like education of high risk groups and health care personnel to reduce the chances for transmission to other. Ensuring the safety of patients by reducing the residual risk of transfusion-transmitted hepatitis is the concern of every transfusion center. Pre-donation counseling, donor self-exclusion and ensuring 100% voluntary blood donation will be effective. Use of disposable syringes for injections and incineration of contaminated material is mandatory.

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Original Article

Burn Injuries

Pattern and Mortality of Burns Injuries in Children

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ABSTRACT

Objectives: To see the type of burns, pattern of burn injuries, burning agent, place of injury and total body surface area involved in children.

Study Design: Descriptive study

Place and Duration of Study: This study was carried out at Burn Unit, Social Security Hospital, Islamabad from January 2006 to March 2014.

Materials and Methods: Children below 16 years of age reporting to causality department with burns were included in the study.

Results: Among 112 patients, 17.85% and 16.96% were from 5 – 6 and 3 - 4 year of age respectively. Flame injuries were commonest (41.07%), followed by hot liquids (31.25%) and electric burns (16.07%). Majority (74.11%) of burn injuries sustained at home. 39.28% and 20.54% sustained less then 10% and 11-20% of burns respectively. Only 8.04% and 5.36% sustained burns between 21-30% and 31-40% respectively. No mortality was observed in patients having less than 40% of burns and 100% mortality among patients having more than 80% burns.

Conclusion: Burn injuries from hot liquid are common in less than 6 years of age and flame burns above 10 years of age while playing with burning shopping bags and working in kitchen. As most of these injuries are avoidable, intensive educational programmes are needed to increase public awareness regarding burn dangers and to teach them how to take proper preventive and safety measures at home.

Key Words: Burns, Children, Etiology, TBSA, Mortality

INTRODUCTION

Burns injury is a major public health problem and is associated with significantly high morbidity and mortality. Children are at high risk because of unawareness and inability to protect themselves. Burns injury in children causes life long imprint on the personality as a result of its sequelae.[1] These injuries represent an extremely stressful experience for both the burns victims and their families. Flame, scald and electric burns are common as a result of domestic and occupational accidents.[2,3] By adopting the proper precautions and safety measures these accidents are preventable in majority of cases. The effectiveness of initial resuscitation, infection control and adequate surgical treatment improves short and long term outcomes.[4] Burns injuries constitute a major concern in the paediatric age group with respect to morbidity and mortality particularly among children in developing countries. To reduce the economical burden of burns injuries, it is necessary to increase current efforts in the prevention of burns injuries.[5] The purpose of the study is to see the type of burns, pattern of burn injuries, burning agent, place of injury and total body surface area involved in children.

MATERIALS AND METHODS

This descriptive study conducted at Burn Unit Social Security Hospital, Islamabad from January 2006 to March 2014. Approval from ethical committee of the hospital was taken.

Social Security Hospital Islamabad is a tertiary care hospital having all necessary facilities for the treatment of burns. All patients with burns injuries less then 16 years of age were included in the study. Informed consent was taken from the parents of the children. All patients reporting to causality were evaluated carefully regarding cause of injury, place of injury, extent of involvement of area burnt and mortality of burn victims. All findings were recorded carefully on a separate Proforma and evaluated statistically at the end of the study by using EPI-6 software.

RESULTS

A total of 112 patients less then 16 years of age were included during the study period. Majority i.e. 20 (17.85) and 19 (16.96%) among them were between age of 5-6 year and 3-4 year respectively (Table-1). Flame injuries were the commonest (41.07%), followed by hot liquid and electric injuries 31.25% and 16.07% respectively. Majority of these injuries were sustained at home (74.11%), followed by outside home or in streets while playing (11.61%). Some 9.82% patients sustained injuries while working i.e. in hotels, shops etc and only 4.46% sustained these injuries during accidents (Table-2). Majority of the patients (39.28% and 20.54%) sustained less than 10% and 11-20% of burns respectively. Only 8.04% and5.36% sustained

burns between 21-30% and 31-40% respectively. More than 90% burns are only noticed in 1.78% of patients (Table-3). No mortality was observed in patients having less than 40% of burns and 100% mortality were noted among patients having more than 80% burns (Table-4).

Table No.1: Different types of burns in different age groups. N = 112

Age Group	Hot liquid	Flame	Chemical		Electric	Others	Total (%)
			Acid	Alkali			
1-2	8	1	-	-	1	-	10 (08.93)
3-4	8	6	-	2	3	-	19 (16.96)
5-6	7	8	-	1	4	-	20 (17.85)
7-8	3	6	-	1	2	-	12 (10.72)
9-10	2	3	-	-	2	2	9 (08.04)
11-12	3	9	-	2	2	-	16 (14.28)
13-14	3	8	1	1	3	1	17 (15.18)
15-16	1	5	1	-	1	1	9 (08.04%)
Total (%)	35 (31.25)	46 (41.07)	2 (01.78)	7 (6.25)	18 (16.07)	4 (03.57)	112

Table No.2: Different types of burns and Place of accident N = 112

	Hot liquid	Flame	Chemical		Electric	Others	Total (%)	Statistics (95% Confidence Limits
			Acid	Alkali				
Domestic	33	30	-	6	13	1	83 (74.11)	69. 35 to 78.92
Street / out side	-	10	-	-	3	-	13 (11.61)	9.23 to 13.41
Occupational	2	4	2	1	2	-	11 (09.82)	7.24 to 11.52
Accidents	-	2	-	-	-	3	5 (04.46)	2.72 to 5.60
Total (%)	35 (31.25)	46 (41.07)	2 (01.78)	7 (6.25)	18 (16.07)	4 (03.57)	112	(Analyzed by Software Epi6

Table No.3: Total body surface area involved in different age groups N = 112

	< 10	11-20	21 - 30	31 - 40	41 - 50	51 - 60	61 - 70	71 - 80	81 – 90	> 90	TOTAL (%)
1-2	6	3	1	-	-	-	-	-	-	-	10 (8.92)
3-4	9	6	2	1	1		-	-	-		19 (16.96)
5-6	8	3	2	1	1	2	1	1	1		20 (17.86)
7-8	5	4	1	-		1	-	1			12 (10.71)
9-10	4	2		1		1	1				9 (8.05)
11-12	4	2	1	1	2	1	1	2	1	1	16 (14.28)
13-14	5	1	1	1	1	2	1	2	2	1	17 (15.18)
15-16	3	2	1	1	1		-	-	1		9 (8.04)
Total (%)	44 (39.28)	23 (20.54)	9 (8.04)	6 (5.36)	6 (5.36)	7 (6.25)	4 (3.57)	6 (5.36)	5 (4.46)	2 (1.78)	112

Table No.4: Total body surface area and Mortality of burns in different age groups N = 112

Body Surface Area	Mortality (%)
0-40 (n = 82)	0 (0)
41-50 (n = 6)	1 (5.55)
51-60 (n = 7)	3 (16.67)
61-70 (n = 4)	2 (11.11)
71-80 (n = 6)	5 (27.78)
81-90 (n = 5)	5 (27.78)
91-100 (n =2)	2 (11.11)

DISCUSSION

Burns injuries are common among children.[1,2] Majority of children's burns injuries are accidental and domestic.[2,6] Incidence varies in different age groups. Incidence is comparatively higher between 1 to 5 years of age because children are more susceptible at this age due to unawareness, curious and active personality.[7] Al-Shehri from Saudi Arabia[3] observed that 54 % of burns victims are between 1 to 5 years of age. Similarly highest incidence below age of 5 years reported from Nigeria,[1] China[8] and Pakistan[9] in different studies. Study done at Singapore General Hospital,[10] Khyber teaching Hospital, Peshawar[11] and JPMC Karachi[12] reported highest incidence below 10 years of age. Similarly in our study highest (34.82%) is noticed in children from 3 to 6 year of age and then again increased frequency (29.46%) is noticed between 11 to 14 years of age. This is probably due to the fact the male children above 10 year of age are more involved in out door activities and female children work in kitchen.

Burns injuries are predominantly domestic in nature.[13] Domestic burns are commonest (86.5%) followed by outside while playing in public as reported by Xin et al.[8] Saleem and his colleagues reported that 89.89% of accidents occurred in home environment, kitchen is the most common place.[9] Similarly in our study domestic burns are common (74.11%), followed by street/ out door (11.61%) and occupational (09.82%). frequency of occupational burns is not reported in developed countries or among those where child labour is prohibited.

Scalds or hot liquids is the commonest cause of burn (51% to 67%) as reported in different international studies.[14,15,16,17] Similarly in Pakistan scalds/ hot liquid is the commonest cause of burns as reported from Karachi[9,12] and Peshawar.[11] In our study, overall flame burns are commonest (41.07%) followed by scalds or hot liquids burns [31.25%]. Majority of our patients with flame burns met this accident in streets commonly with burning shopping bags or at home while busy in cooking in kitchen. In our study prevalence of scalds is more common below 10 years of age which is also observed in other studies.[3,14,18] Whereas above 10 years of age flame burns are more common because majority of our girls help their mothers in kitchen during cooking or involved in independent cooking at home. Incidence of flame burns varies i.e. 26.8% from Nigeria, 27.6% from Saudi Arabia,[3] 28.4% from Israel[14] and 35.2% from Singapore.[10]

Electric burns are third most common cause (16.07%) in our patients. Electric burns are usually from domestic set up while handling the electronic equipment and playing with power plugs. Other causes of electric burns are accidental contact with non insulated wires on electric poles while playing at roof top and during kite flying. In literature, 5 % cases due to electrical burns reported by Al-Shehri[3] and 3% by Uba and his colleagues.[18] In our setup frequency is comparatively high probably due to non insulated wires on electric poles in our streets and lack of awareness and preventive education of children.

Chemical burns are uncommon as observed in our study. Among chemical burns alkali is more common cause of burns (6.25%) as compared to acid. Alkali burns are more commonly reported in literature as compared to acid burns. [2,3,19] Reason for this is probably due to the fact that alkalis are commonly used in domestic set up e.g. washing clothes and cleaning of different items. These products are usually found in home and children sustain burns while handling them in mistake for other liquids. In contrary from China, chemical burns are second commonest cause after scalding as reported by Xin et al.[8]

Burns due to explosives are uncommon as observed in our study and in literature. The most common cause of explosive burns is handling of marriage bombs and different explosives usually used during different religious and local festivals.

In our study majority of patients (59.81%) sustained less than 20% burns and only 1.78% children sustained more than 90% burns. Burns in children are usually less severe because they are commonly inflicted in domestic setup and in restricted environments.[20] In Israel 94% children develop less than 20% burns.[14] Where as another study from National Institute of Child Health, Karachi Pakistan shows that 62% of cases Total Body Surface Area burnt was less than 30%.[9] Same observation was made by Xin et al[8] and Al- Shehri.[3]

Overall 16.70% mortality is noticed in our study and majority among them having more than 70% of burns. Mortality is almost 100% among patients having more than 80% burns. Commonest cause of mortality is sepsis in our patients. Mortality among our patients is quite high as compared to international literature. Studies shows 0.7% mortality from Israel,[14] 1.15% from China[4] and 4.61% from Singapore.[10] This high mortality is due to inadequate health resources especially lack of specialized burns units and staff even at tertiary level hospitals in our setup.

CONCLUSION

It is concluded that burns injuries from hot liquids are

common in less than 6 year of age. In children above 10 year of age flame burns are common while playing outdoor especially with burning shopping bags and while working in kitchen. As most of these injuries are avoidable so intensive educational programmes are needed to increase public awareness regarding nature and danger of burns. It is also important to teach the children and parents how to take proper preventive and safety measures at home and while playing outdoor..

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Original Article

Children Infected with Staphylococcus

Comparison of Duration of Hospitalization and Clinical Outcome in Children Infected With Methicillin Resistant Staphylococcus Aureus and Methicillin Sensitive Staphylococcus Aureus

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ABSTRACT

Objective: To compare the duration of hospitalization and clinical outcome in children infected with methicilline-sensitive staphylococcus aureus and methicillin-resistant Staphylococcus aureus.(MRSA and MSSA)

Study Design: comparative cross sectional

Place and Duration of Study: This Study was carried out at the Paediatrics Department, Nishtar hospital Multan from 14.01.2012 to 13.07.2012

Materials and Methods: Children meeting the inclusion criteria were selected. Clinical samples were collected before starting antibiotics and sent to microbiology lab for culture. Colony morphology, gram straining and production of catalase and coagulase . confirmed growth of S. aureus. Methicillin resistance was determined by disk diffusion method according to CLSI guidelines. S.aureus with inhibition zone more than 18 mm were taken as methicillin-sensitive and those inhibition zone of less than 18 mm were taken as methicillin-resistant. Adequate information regarding identification of patient, clinical diagnosis, duration of hospital stay and clinical outcome were entered . Aftertaking consent from parents.Lab results were entered in the proforma.

Children of all age groups up to 12 years of age and both sexes were included to avoid any bias. All patients clinically diagnosed to be suffering from staphylococcal infection (septicemia, pneumonia, skeletal infection, skin & soft tissue infection, meningitis) who were admitted in pediatric ward were included.

Results: Sixty patients with S. aureus infection were included in the study. Thirty patients were of MRSA and 30 were of MSSA. In MRSA group 12 (40%) patients remained in the hospital for less than a week and 18 (60%) patients stayed for more than a week but less than 3 weeks. In MSSA group 23(76.6%) patients were hospitalized for less than one week duration and 7(23.4%) patients were admitted for more than 1 week but less than 3 weeks duration. In MRSA group, 15(50%) patients recovered, 4(13.4%) patients improved, 2(6.6%) patients didn't improved and 9(30%) patients expired. In MSSA group, 22(73.4%) patients recovered completely, 4(13.4%) patients improved, 2(6.6%) patients didn't improved and 2(6.6%) patients expired.

Conclusion: Children suffering from MRSA infection have more severe illness as compared to those suffering from MSSA infection. Duration of hospitalization of children suffering from MRSA infection is prolonged as compared to MSSA infection while clinical outcome is better in children suffering from MSSA infection as compared to MRSA infection.

Key Words: Methicillin-resistant Staphylococcus aureus, MSSA

INTRODUCTION

Staphylococcus aureus is a very common cause of infection in all age groups, diseases produced by S. aureus in children include skin & soft tissue infection, abscesses,wound infections, neonatal sepsis, toxic shock syndrome, staphylococcal Scalded skin syndrome and food poisoning.[1]

S.aureus gets colonized on the body surface of newborns within first week of life through transmission by direct contact. S.aureus is also present in anterior nares of 20-30% of normal individuals. Invasive disease follows colonization in susceptible individuals.[2]

Staph.aureus is becoming increasingly difficult to treat these days. In 1944 when Penicillin was introduced, over 95% of staphylococcus isolates were susceptible to the drug. Slowly penicillin resistance emerged. In 1959 introduction of beta lactamase stable antibiotics, methicillin, cloxacillin and flucloxacillin, briefly overcome this resistance. However by early 1970 Methicillin resistant Staphylococcus aureus (MRSA) emerged.[3]

S.aureus strains that are sensitive to B-lactamase-resistant penicillins are called methicillin-sensitive S.aureus (MSSA). Strains of S.aureus that are resistant to the B-lactamase resistant penicillins such as methicillin and nafcillin, are commonly known as methicillin resistant S.aureus(MRSA). Community associated methicillin resistant S.aureus (MRSA is a

dangerous pathogen that is difficult to treat and has been associated with increasing fatality in children and young adults worldwide.[4]

The aim of this study is to find out the difference between duration of hospitalization and clinical outcome in children infected with methicillin-resistant S.aureus (MRSA) and methicillin sensitive S.aureus (MSSA).

MATERIALS AND METHODS

This comparative cross sectional was carried out at Paediatrics Department, Nishtar Hospital Multan from 14-01-2012 to 13-07-2012.

Before starting the study, permission from the ethical review committee of the Hospital was taken. Standard antibiotics and other supportive treatment were provided to the hospitalized children included in the study. This study was without any harm to participating patients.

Children of all age groups up to 12 years of age and both sexes were included in the study to avoid any bias. All patients clinically diagnosed to be suffering from staphylococcal infection (septicemia, pneumonia, skeletal infection, skin & soft tissue infection, meningitis) were admitted in pediatric ward.

Adequate information regarding identification of patient, clinical diagnosis, duration of hospital stay and clinical outcome were entered in a pre-designed proforma after taking consent from the parents. Laboratory results were entered in the proforma.

Blood, pus and any collection of fluid like pleural fluid were drawn before starting the antibiotics and sent to microbiology lab for culture. Colony morphology, gram staining and production of catalase and coagulase confirmed growth of Staph. aureus.

Confirmed growth of S. aureus. Methicillin resistance was determined by disk diffusion method according to CLSI guidelines. S.aureus with inhibition zone more than 18 mm were taken as methicillin-sensitive and those inhibition zone of less than 18 mm were taken as methicillin-resistant.

Data was entered into SPSS version 10. Descriptive statistics were used to describe the variables in both groups. Mean and standard deviation of age, hemoglobin and leukocyte count were assessed. Proportion of patients belonging to different categories in address, source of infection and clinical diagnosis were assessed .The duration of hospital stay and clinical outcome were compared in both groups to draw the results. During comparison of variables student's t-test was used to compare numerical variable e.g. age and duration of hospital stay and chi-square test was used to compare categorical variables e.g. source of infection, clinical diagnosis and clinical outcome. Level of significance (p-value) was taken at 0.05.

RESULTS

Sixty children with positive S.aureus infection were included in this study All the patients were divided in to two groups; methicillin resistant S.aureus. (MARSA) and methicillin sensitive S.aureus (MSSA) groups. In each group there were 30 patients. Results of the study according to variables are below.

70% patients were less than one month of age in MRSA group and 56.7%patients were in MSSA group which were less than one month 20% patients were between the age of 1month- 5 years in MRSA group. While this number was 16.6% in MSSA group. 10 % patients were the age between 6 years- 12 years in the former group while this number was 16.6%in the later group.

In MRSA group 66.6% patients were male while this figure was 60% in MSSA group 33.4% patients were female in the former group while these 40% patients in the later group.66.6% patients were in MRSA group came from urban areas while 33.4% patients belongs to rural area in this group. In the MSSA group 40% patients belong to rural area in this group. The MSSA group 40% patients were from urban areas while remaining 60% patients came from rural areas.

Table No.I: Source of infection n=60.

Source	MRSA	%age	MSSA	%age
Community Acquired	17	56.7%	23	76.7%
Hospital Acquired	13	43.3%	7	23.3%
Total	30	100%	30	100%

P-value = 0.006

Table No.2: Clinical diagnosis n=60.

Diagnosis	No. of Patients of MRSA	%age	No. of Patients of MSSA	%age
Septicemia	19	63.4%	14	46.7%
Pneumonia	08	26.6%	11	36.7%
Skin&Soft Tissue Infection	02	6.6%	03	10%
Skeletal Infection	0	0%	01	3.3%
Meningitis	01	3.3%	0	0%
Other sites	0	0%	0	3.3%
Total	30	100%	30	100%

Table No.3: Duration of hospitalizationn=60.

Duration	MRSA	%age	MSSA	%age	p-value
< 7 Days	12	40%	23	76.6%	0.04
7-21 Days	18	60%	7	23.4%	0.02
Total	30	100%	30	100%	

Table No.4: Clinicaloutcome of patients n=60.

Outcome	MRSA	%age	MSSA	%age
Recovered	15	50%	22	73.4%
Improved	4	13.4%	4	13.4%
Not Improved	2	6.6%	2	6.6%
Expired	9	30%	2	6.6%
Total	30	100%	30	100%

P-value (by comparing alive and expired) = 0.001

DISCUSSION

Among 60 patients of our study (30 from each group); age, gender and type of infection of the patients in two groups were similar. Among source of infection, majority of the patients (66.6%) were having community acquired infection while the remainders (34.4%) were having nosocomial infection. Among nosocomial infection, majority (65%) was of MRSA type and the remaining revealed MSSA on culture; p-value = 0.006.

Duration of hospitalization was more prolong for MRSA group as compared to MSSA group (Eighteen patients from MRSA group remained for more than 7 days but less than 21 days duration in hospital as compared to MSSA groupin which seven patients remained in the hospital for the above mentioned duration; p-value= 0.02 Twelve patients from MRSA group remained from less than 7 days duration while this number was 23 for MSSA group; p-value =0.04). Regarding outcome, it was better for MSSA group as compared to MRSA group (Nine patients from MRSA group expired and remaining were alivewhile two patients expired in MSSA group and the remainder werealive in this group; p-value =0.001)

Romero-Vivas et al.,[5] whoconducted the largest study, noted a significantly higher fatality rate among patients with MRSA bacteremia(58.3% for MRSA group as compared to 32% for MSSA group = p<0.01).More recently, Conterno et al.,[6] Also reported methicillin resistance as a risk factor for a poor outcome in patients with Staph. aureus bacteremia.

In another study conducted by Skiest DJ et al.,[7] at The University of Texas Southwestern Medical Center, Dallas, USA, patients with MRSA most commonly presented with a skin or soft tissue infection: 69 % versus 45% p=0.0012 while patients with MSSA were more likely to have infection of the respiratory tract: 11% versus 3%, p=0.02. They also noted that most patients with MRSA infection did have used antibiotics in the last six months.

According to Rozgonyi F etal.[8] numerous studies have indicted, based on mortality rates, that methicillin-resistant Staphylococcus aureus (MRSA)strains are more virulent than methicillin-sensitive Staphylo-coccusaureus (MSSA) strains.

A study conducted by Miller R et al.,[9] at Nuffield Department of Medicine, University of Oxford, John Radcliffe Hospital, Oxford, UK, says that clinical presentation of MRSA and MSSA bacteremia was similar. The patients admitted with MRSA bacteremia had significantly higher levels of previous hospital exposure than patients with MSSA infection and also had more co-morbidities as compared to MSSA infection.

In contrast to our study, in a review of Staphylococcus aureus infection, Dr. Lowy.,[10] stated that bacteremia involving methicillin-resistant Staphylococcus aureus (MRSA) is not associated with higher mortality than bacteremia involving methicillin-sensitive Staphy lococcus aureus.

CONCLUSION

This study showed higher mortality rate with MRSA infection than infection with MSSA strains of Staphylococcus aureus. It also showed that duration of hospitalization was prolonged in patients with MRSA infection as compared to MSSA group.

Recommendations: Infection with Staphylococcus aureus in patients admitted to our hospitals is of serious concern and many patients admitted with sepsis or pneumonia have Staphylococcus aureusas the cause of their morbidity.

Majority of the patients with MRSA infection, acquire their microbe from hospital environment. So, there is dire need to adopt basic principles of asepsis and sterilization; most importantly hand washing.

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Original Article

Small Bowel Obstruction

Current Pattern and Diagnosis of Small Bowel Obstruction in the Patients of Rural Areas

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ABSTRACT

Objective: Objective of this study to determine the clinical presenting factors including diagnosis and risk factors of the patients those admitted with small bowel obstruction.
Study Design: Observational study
Place and Duration of Study: This study was carried out at the Departments of General Surgery, Peoples Medical University and Health Science Nawabshah and Isra University Hospital Hyderabad from March 2013 to Aug 2013.
Materials and Methods: After admission detailed history, physical examination, ultrasound, X-ray abdomen erect and supine and all routine baseline laboratory investigations were carried out. CT scan was done in the selected patients. Final diagnosis was done by laparotomy which was attempted after thorough initial assessment and investigations.
Results: Total 50 patients were included in the study of the rural areas of the Sindh, from all of them male were in majority. On the clinical presenting features Nausea, Constipation and Abdominal pain were most common with the percentage of 92%, 80% and 78% while other presenting features as; Vomiting, Abdominal tenderness, Abdominal distension, Fever, Epigastrium pain, Rectal bleeding and Rebound tenderness were with the percentage of 40%, 42%, 22%, 38%, 30%, 16%, 10% and 26% respectively. On the diagnosis adhesion was found as most common.
Conclusions: In the conclusion of this study adhesion found as most common and leading cause of small bowel obstruction.
Key Words: Asthma, Triggers, Children

INTRODUCTION

Small bowel obstruction is a very common surgical emergency.[1] It is estimated for 20% of surgical admissions[2] and is a very common cause of morbidity almost the world.[3] Successful treatment contains early and perfect diagnosis.[4] The complete diagnostic methodology regarding history, radiological investigation and physical examination.[5] CT scans are supposed to have superior assessment and the aid treatment of bowel obstruction having newly increased more popularity.[6] While CT has showed very great efficacy in identifying the small bowel obstruction, according to the reports of studies a sensitivity great as 93%, the specificity of equal to 100% and accuracy round about 94% in the diagnosis small bowel obstruction,[7] some reports showed that more significant role of CT scans lies in demonstrate etiology and severity of obstruction slightly than diagnosing of it.[8] CT scans can exactly shows the sits, severity and level of obstruction[9] and also been shown to be sensitive for signs of the strangulation and volvulus.[10,11] According to Etiology the patterns of intestinal obstruction had changed over the years. In 1920s hernias were responsible for 50% intestinal obstruction of the cases and 7% adhesions.[12] Now a day's adhesions are accountable for 65% of the cases.[3] Therefore intestinal obstructions due to adhesion supposed as diagnosis of exclusion till the now.[8] The commonest limitation of the CT scans is its inability to evaluate the adhesions.[7] In the Pakistan, where health care resources are already limited and peoples are the self financed, the CT scan represents a significant undertaking. It is hypothesized that CT scans with the great accuracy at diagnosing mechanical bowel obstruction. Purpose of this to determine the clinical presenting factors along with diagnosis and risk factors of the patients those admitted with small bowel obstruction at surgical unit of Peoples University Hospital Nawabshah.

MATERIALS AND METHODS

This observational study was contains 50 patients and was carried out at peoples medical university and health science Nawabshah and Isra University Hospital Hyderabad. All the patients of rural areas of the sindh were included in the study. Study was carried out with the duration of six month from March 2013 to Aug 2013 at the department of general surgery. All the patients with small bowel obstruction on the basis of singe and symptoms were selected and admitted for the complete diagnosis. After admission detailed history, physical examination, ultrasound, X-ray abdomen erect and supine and all routine baseline laboratory

investigations were carried out. CT scan was done in the selected patients. Final diagnosis was done by laparotomy which was attempted after thorough initial assessment and investigations. A written consent was taken from all the patients and also counseled all the patients from risk of the disease. All presenting features cause and diagnosis were noted on the Performa. Data was analyzed on SPSS program version 16.0.

RESULTS

Total 50 patients were included in the study, from all of them male were in majority 64% as compare to females 36%. Most common age group was 32-45 of the age with 44%; second most common age group was 15-30 years of the age. Table No. 1.

On the clinical presenting features Nausea, Constipation and Abdominal pain were most common with the percentage of 92%, 80% and 78% while other presenting features as; Vomiting, Abdominal tenderness, Abdominal distension, Fever, Epigastrium pain, Rectal bleeding and Rebound tenderness were with the percentage of 40%, 42%, 22%, 38%, 30%, 16%, 10% and 26% respectively. Table No. 2.

On the diagnosis adhesion was found as most common 49% while other diagnosis were as, obstructed hernia, abdominal TB, volvulus, malignancy, Ischaemia, intra abdominal abscess, perforation and ilial stricture with the percentage of 5%,3%,35,10%, 8%,6% and 9% respectively. Figure No.1

Table No.1: Basic characteristics of the patients (n=50)

Characteristics	No of patients/ percentage
Male	32/ (64%)
Females	18/ (36%)
Age groups	
15-30	16/ (32%)
31-45	22/ (44%)
46-60	10/ (20%)
<60	02/ (4%)

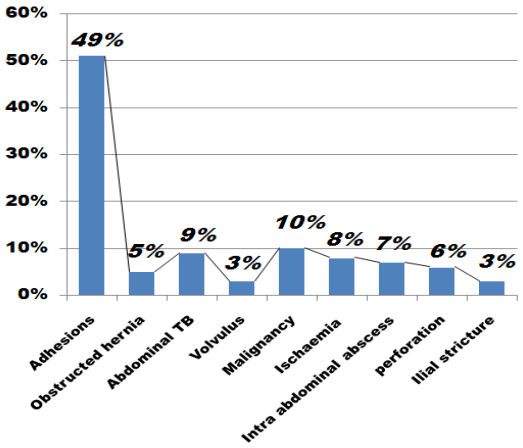

Figure No.1: Diagnosis/ causes of obstruction. N=50

Table No.2: Clinical features of the patients. (n=50)

Features	Frequency	%age
Constipation	40	80%
Vomiting	20	40%
Abdominal pain	39	78%
Abdominal tenderness	21	42%
Abdominal distension	11	22%
Fever	19	38%
Epigastrium pain	15	30%
Rectal bleeding	08	16%
Nausea	05	10%
Rebound tenderness	46	92%
	13	26%

DISCUSSION

Small bowel obstruction is one of the major surgical emergencies. In the present study male were in majority 64% as compare to females 36%. Most common age group was 32-45 of the age with 44%; second most common age group was 15-30 years of the age. Similarly in the study of Naseer Ahmed Baloch et al,[13] reported that male were in the majority and the mean age of the patients was 37.4. Similar results were also found in the study of Safir Ullah et al.[14]

In the above mentioned study of Naseer Ahmed Baloch et al,[13] reported clinical presentation as; abdominal pain, vomiting, constipation, abdominal distension, abdominal tenderness, rebound tenderness, fever, shock, weight loss and bleeding per rectum with the percentage 95.2, 88.9, 84.1, 79.4, 82.1, 82.1, 12.3, 55.2, 39.3 and 23.4 respectively, as well as in the present series nausea, constipation and abdominal pain were most common with the percentage of 92%, 80% and 78% while other presenting features as; vomiting, abdominal tenderness, abdominal distension, Fever, epigastrium pain, Rectal bleeding and Rebound tenderness were with the percentage of 40%, 42%, 22%, 38%, 30%, 16%, 10% and 26% respectively. Clinical features of the Muhammad Saleem Sheikh et al,[15] can be compared with this study.

According to Muyembe[16] five leading causes of intestinal obstruction in Nyeri, Kenya, are: sigmoid volvulus, external herniae, adhesions and bands, ileocolic intussusception and small bowel volvulus. Another study from a developing country has described adhesions (75%) and neoplasms (11%) to be the most common causes.[15] From Greece has described Adhesions, hernias, and large bowel cancer to be the most common causes of intestinal obstruction.[17] In the present series adhesion was found as most common 49% while other diagnosis were as, obstructed hernia, abdominal TB, volvulus, malignancy, Ischaemia, intra abdominal abscess, perforation and ilial stricture with the percentage of 5%,3%,35,10%, 8%,6% and 9% respectively. Many local conducted in Pakistan have different reports, according to Mehmood Z et al[18], Ismail et al[19], Zahra T et al,[20] reported that Tuberculosis

is the most common cause of intestinal obstruction. Others [21-23] have mentioned that only mechanical bowel obstruction according to their studies and they have also reported that adhesions and tuberculosis to be the most common causes in their studies respectively. According to Jehandgir et al[24] mentioned that hernias and adhesions were the most common cause of obstruction.

CONCLUSION

In the conclusion of this study adhesion found as most common and leading cause of small bowel obstruction, mostly cases of this study were late diagnosed because they belongs with rural areas where good medical facilities are very short. This should be quick diagnosed to prevent the increased morbidity and mortality, in the condition of delay in the diagnosis of mortality rate can increase.

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Original Article

Perinatal Mortality

Perinatal Mortality: A Mirror Image of Maternal Health

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ABSTRACT

Objective: Perinatal mortality usually reflects health status of mother and is indicator of quality of care received by mother during her period of gravidness and fetus at birth. We carried out this study to evaluate the magnitude of perinatal mortality at our institute and its contributing factors
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted at Obst. & Gynae Unit II and Unit of Pediatric Medicine, Chandka Medical College hospital Larkana from 1st January 2012 to 31st December 2012.
Materials and Methods: Women who delivered after 24 completed weeks were selected from labour room. Perinatal deaths including stillbirths and early neonatal deaths up to 7 days of life were studied. Outcome variables like maternal age, parity, communal standing and booking status were taken in to consideration. Complications arising during pregnancy or any medical illness, details of labour, fetal condition at birth were also noted.
Results: During the study period 4818 women delivered. There were 473 perinatal deaths with a perinatal mortality rate of 98/1,000 live births. Among these women only 9% were booked, while 91% un-booked. Perinatal death rate was more seen in maternal age group between21-30 years that were 51%. Women having parity of 2-5 had highest perinatal mortality of about 44%. Gestational age from 31-36 weeks contributed about 46%. Most prevalent condition reportedly causing perinatal death was prolonged and obstructed labour which added 30% of total, followed by antepartum hemorrhage causing 18% of perinatal deaths. Hypertensive disorders and other maternal medical diseases contributed about 15.5% and 6.5% respectively.10% fetuses died of congenital anomalies.11% neonatal septicemia seen. Unexplained still births seen in 9% of total.
Conclusion: Perinatal mortality is stagnantly high among mothers with poor health even having no access for antenatal, intra partum and postnatal care. Unfortunately they report to hospital when already had developed some complication. Awareness programs at community level, training health workers providing facilities at remote health centers can make the lot of difference.
Key Words: Perinatal mortality, Still birth, Early neonatal death.

INTRODUCTION

Perinatal mortality (PNM) is defined as the death of a fetus from 24 completed weeks of gestation up to first 7 days of life after birth. It embraces all intrauterine, intrapartum deaths, stillbirths and early neonatal deaths up to seven days of life.[1] PNM is the root to analyze the perinatal mortality rate which is extracted out of 1000 live births. Perinatal mortality is a universal problem leaving perinatal death number as high as 59 lacs throughout the world every year and among them10 lacs babies had intrapartum deaths paralleling 11 deaths each minute.[2]This scenario is upsetting under developed countries more than developed part of world especially those in sub-Saharan Africa and south central Asia.[3]Pakistan is a developing country where women are rarely coming for antenatal visits and even 68% births take place at home without realizing availability of resources required for diagnosing fetal compromise and for neonatal resuscitation.[4] Truth is that most perinatal deaths in our society are not reported but roughly it has been estimated that in Pakistan every year about 5.3 million babies are born and sadly among them 5.09%(2,70,000) new borns die.[5] 2013 report of international agency has ranked Pakistan on the top of countries having high still birth and neonatal death rate which shows as 1 million babies die on first day of life and another 1.2 million are stillbirths. [6]Reduction in these deaths necessitates the monetary, social and governmental drive to gadget widespread ingress to good class care during pregnancy, childbirth and neonatal period as death ratio is direct reflection of care provided to mother.[2] This is even possible with simple measures like from Pakistan, one cluster- randomized controlled trial of training of traditional birth attendants claimed 30% reduction in frequency of perinatal deaths just with 3 days training on basic ante and intrapartum care, clean safe delivery with disposable delivery kits and referring complicated cases for neobon care [7] with another study showing high institutional deliveries with maternal voucher scheme.[8]
Chandka medical college hospital is a tertiary care hospital of upper Sindh with wide catchment area up to borders of Baluchistan and Punjab. Doing this study was aimed to find out the frequency of perinatal deaths (PNDs), its causes or risk factors and to recognize avertible factors.

MATERIALS AND METHODS

It was an observational cross sectional study conducted from 1st January 2012 to 31st December 2012 at departments of Obstetrics and Paediatrics of Chandka

Medical College Larkana. All patients who delivered beyond 24 weeks of gestation were included in the study. Perinatal deaths involving still- births either fresh or macerated stillbirths were registered. Neoborns whichever died in obstetric ward or in the department of Pediatrics(referred from obstetric ward) up to seven days of life were listed in our study. Those with <24 weeks pregnancy were excluded. Age, parity, gestational age and social status of all mothers noted down. Mode of delivery, complications developing during pregnancy, any medical disorder causing problem to mother or fetus and other relevant factors were assessed. Fetuses explored for congenital anomaly as well. Ethical approval and clearance was obtained from Chandka Medical College Institutional Review Board (IRB).Informed consent obtained. Moreover, privacy and secrecy was assured by evaluating and circulating the findings in aggregate.

RESULTS

During the study period of one year from January to December 2012, there were 4818 deliveries. Among them 473 perinatal deaths occurred with a perinatal mortality rate of 98/1,000 live births. Looking at booking status of these women, just only 9% were booked. While 91% were un-booked. Perinatal death rate seen in maternal age group between21-30 years was 51%. Multiparous women having parity of 2-5 had seen higher perinatal mortality 44% in this study. Fetuses group having gestational age from 31-36 weeks contributed about 46% also detailed in table 1.

Table No.I: Characteristics of maternal history

Characteristics	Percentage
Un-booked	91%
Booked	9%
Age group	
15-20 years	11%
21-30 years	51%
31-40 years	21%
More than 40 years	17%
Parity	
Para 0-1	23%
Para 2-5	44%
Para >5	33%
Gestational age	
31-36 weeks	46%
24-30 weeks	22%
37-42 weeks	32%

Most prevalent condition reportedly causing perinatal death was in our setup prolonged and obstructed labour which added 30% of total, followed by antepartum hemorrhage causing 18% of perinatal deaths. Hypertensive disorders and other maternal medical diseases contributed about 15.5% and 6.5% respectively. 11% fetuses died of congenital anomalies. 9% neonatal septicemia seen. Unexplained still births seen in 10% of total also shown in table 2 with their mode of delivery. Fetal condition at birth whether stillborn or number of early neonatal deaths and perinatal mortality rate is elicited in table 3.

Table No.2: Obvious Causes of Fetal and Neonatal Death and their Mode of Delivery.

Causes	Number	Percentage
Mechanical problems	142	30%
Antepartum hemorrhage	85	18%
Hypertensive disorders	74	15.5%
Congenital anomalies	52	11%
Unexplained deaths	47	10%
Neonatal septicemia	42	9%
Maternal medical problems	31	6.5%
Type of delivery		
Cesarean section	227	48%
Assisted vaginal delivery	86	18%
Spontaneous vaginal delivery	160	34%

Table No.3: Perinatal deaths rate in relation to total deliveries at CMCH

Variable	Number
Total number of deliveries	4818
Total number of still births	378
Total early neonatal deaths	95
Perinatal mortality rate	98/1,000
Still Birth rate	79.9/1,000
Early neonatal death rate	20.1/1,000

DISCUSSION

Perinatal mortality is a sad event in mothers life, who after keeping baby for long nine months in womb, get nothing in her lap. In our study perinatal mortality rate (PNM) rate was 98/1,000, which is parallel to other studies .A study conducted in the city of Hyderabad Sindh province of Pakistan, having same social environment showed PNMR even greater than our study as 100/1000, [9]while metropolitan city hospital shared almost same figures 97.2/1000 as we had in our setup.[10]We cannot compare our results with industrialized countries like England and wales where PNMR is very low [11, 12]

Pakistan being a developing country although many intervention are done but still it is having rate of perinatal mortality still high as 68-81/1,000 in connotation to other developing countries even of South Asia like India and Bangladesh.[6]

PNM is an indicator to weigh the worth of health care provision and is definitely affected by social, ethical, economical and scholastic values of areas, where mother is living. A huge figure of pregnant women unfortunately do not even turn for antenatal care rather they report to hospital once they have developed

obstetrical complications, which again is reason for high PNM rate. In our study there were 91.7% cases women were un booked of PNM without any antenatal care. This has been agreed internationally as elicited in study done in Nepal, where they found 16 times more perinatal mortality in group of women having no antenatal care.[8,13] Another study done by pediatricians in Pakistan′s biggest city also clearly mentioned effects of maternal status on perinatal mortality rate as neither these women are evaluated for any risk factor prenatally nor they have home delivery by skilled persons which results in undesirable fetal outcomes.[14] Perinatal outcome may be adverse in extreme of ages, but in our study it was age group of 21-30 years, which was affected with poor perinatal ending because this age group takes high domestic responsibilities and does not pay heed to their own requirements. This finding is mirrored in other studies as well.[9, 15]

Although many studies are showing worsening perinatal outcome in grand multiparous mothers, [16, 17] women but we had the finding of adverse pregnancy outcome in women having parity between 2-5 and these multiparous women are over projected that they have previous experience of pregnancy and childbirth, so they may not develop complications. Our country where most people are living below poverty line sensitization is more needed to improve maternal health status subsequently decreasing PNMR. Same conditions are prevalent in African countries, so is reported in study done in far and deprived area. [18]

Larkana had to face natural disaster in 2010 with flood damaging properties of people so making them economically under privileged forcing them back to live in areas with limited resources and this has directly affected lives of pregnant women. We found in our study underutilization of obstetrical services in such poor women with financial and geographical constraints made them to report late at tertiary care hospital after long length of labour with the diagnosis of prolonged and obstructed labour which caused 30 % of intra and neonatal deaths of fetuses. Same type of scenario with increased perinatal mortality is shared by studies done by studies from Pakistan [19], Bangladesh[20] and Ethiopia, [18] while study done at Abbottabad Pakistan concluded abnormal labour as 3rd frequent cause of pnm where it was 18% perinatal mortality due to prolonged and obstructed labour.[17]

The association is, if those females who had perinatal fetal deaths due to mechanical factors like

malpresentation and obstructed labor, were provided optimal intrapartal care, almost all babies could have been salvaged, and no mother should have developed rupture in unscarred uterus. Antepartum hemorrhage was second commonest cause of perinatal mortality in our setup that was 18% and nearly same has been conveyed in a study conducted by Indian author.[21] Looking in to causes of still birth. This also reflects the attitude of community. Had they utilized services of at least skilled birth attendants or lady health workers, most of babies would have been able to survive in this world as seen in figures quoted by Bhutta et al.[22]

Hypertensive disorders of mothers ranged up to 15.5% as a causative agent for perinatal mortality in current study which may be below real figures as many of mothers get delivered then and there without knowing the cause and they just share in their history while facing same event in subsequent pregnancy, especially multiparous women also pronounced in literature.[23] Other medical disorders made their contribution up to 6.5% in our ward perinatal mortality which were quite treatable and avoidable conditions. Terrible thing is that people who have some problem during pregnancy don't seek treatment as they consider "pregnancy as an act of mother nature which should not be hindered" and regrettably this group had perinatal mortality three time more than general public.[24] Congenital birth defect have been seen up to 11% of perinatal deaths in our data and almost near to it 8% communicated by another South Asian study.[25]

Noninvasive diagnostic tool ultrasound is very least used by people living in far side. Had they used fearlessly, frequency of stillborn at birth would have been decreased and information obtained from ultrasound would have given insight for prevention of congenital defects. Despite having postmortem of still babies in country like Norway, researchers were of opinion that one fourth of still births remain unexplained and same happened in our study though we did not go for postmortem in our setup but it can help identification of some identifiable causes.[26] Neonatal sepsis seen up to 9% in our circumstance, which is indication of unsupervised prolonged labour and manipulation by un trained attendants may not be comparable to other hospitals.[17]

CONCLUSION

We are about to enter in 2015, which was made as targeted year to achieve Millennium development goal (MDG 4 and 5) for reducing perinatal and maternal mortality. Though lots of agencies are doing their best to achieve the target but yet vigorous efforts to be taken to get optimum results. It requires sensitization of community, motivation and empowerment of mothers and folks to decide for exercising their right to have supervised preventive as well as emergency care in health facilities because of direct influence of maternal health on perinatal endings.

Ownership and partaking of stake holders in particular areas have reflected difference in the form of more institutional deliveries and subsequent improvement in fetomaternal outcome. Same should be practice everywhere. There is pressing need to expand infrastructure on the way to hospital, ambulance services and of course availability of trained and skilled

persons in nearest health facility to obtain successful outcomes.

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Original Article

Biochemical changes in Schizophrenics

Inter-Relationship of Circulating Biochemical Markers of Oxidative Stress and Thyroid Hormones in newly Diagnosed Schizophrenics: Perspective study from Local Population of Punjab Pakistan

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ABSTRACT

Objective: Current study was conducted to determine the fluctuations of various circulating biomarkers including thyroid hormones, hepatic enzymes, oxidative stress markers as well as electrolytes in schizophrenics.

Study Design. Cross Sectional Study.

Place and Duration of Study: This study was conducted at Psychiatric Clinic of Jinnah Hospital, Mental Hospital from Jan. 2013 to Oct. 2013.

Materials and Methods: Seventy five acute schizophrenics and twenty five healthy individuals were selected for this study. Patients with chronic infections, diabetic history, liver disease or any other history of drugs including smoking and/or drinking alcohol were excluded from the study.

Results: Elevated levels of oxidative stress in the form of malondialdehyde (MDA) (7.8±2.71*) were observed in schizophrenics. Similarly raised levels of T3 (6.9±1.31*) and T4 (61.2±15.44*) were found in patients as compared to control. Electrolytes like Na, K, Ca and Mg showed alterations in the serum of both patients and control.

Conclusion: All the circulating biochemical markers were statistically significant (P<0.05). It is concluded that lipid peroxidation may has association with thyroid hormones and electrolytes. Moreover, alleviated concentration of anti-oxidant biomarkers like SOD, catalase and GSH may play a central role in schizophrenics and anti-oxidant therapy may be useful for the management of this psychiatric disorder.

Key Words: Oxidative Stress,Thyroid Hormone,Schizophrenia,Anti-Oxidant,Malondialdehyde,SOD,Catalase, GSH

INTRODUCTION

Schizophrenia is one of the most important mental disorders associated with dysfunction in brain structure and function, neurological abnormalities as well as physical anomalies. Long term memory and working memory are affected due to brain abnormalities. Schizophrenia usually characterized by disturbances in social behavior, emotional reactions and thinking associated with hallucination as well as illusions. Association of schizophrenic patients has been proposed with malnutrition, immune activation, obstetric complications and maternal exposure to stress. Alterations in the level of various neurotransmitters like dopamine in schizophrenic patients have been associated with delusions and hallucinations.

One of the important factors related to the pathological condition is oxidative stress in the biological system and it is also associated with patients suffering from schizophrenia [1](Akiibinu et al., 2012; [2]Ong et al., 2010). Similarly, alterations in thyroid hormones are common in mental disorders (Akiibinu et al., 2012; [3](Yazici et al., 2002), because particular concentration of thyroid hormones is crucial for maturation and development of central nervous system.

Current study was conducted to determine the fluctuations of various circulating biomarkers including thyroid hormones, hepatic enzymes, oxidative stress markers as well as electrolytes in schizophrenics.

MATERIALS AND METHODS

Seventy five (75) individuals suffering from acute schizophrenia, attending Psychiatric clinic in Jinnah Hospital, Lahore were included in this study. Only those patients were included that were not taking any treatment for schizophrenia. Patients with chronic infections, diabetic history, liver disease or any other history of drugs including smoking and/or drinking alcohol were excluded from the study. Moreover, twenty five (25) healthy individuals served as control group.

Following parameters were estimated

I-Lipid profile (Total Chol., Tg, HDL and LDL)

II-Electrolytes profile (Ca, K, Mg and Na)

III-Stress biomarkers including malondialdehyde (MDA)[4](Ohkawa et al., 1979), superoxide dismutase (SOD)[5] (Kakkar et al., 1984), catalase (Aebi, 1974), reduced glutathione (GSH) [6](Moron et al., 1979).

IV- Thyroid hormones (T3, T4 and TSH) were evaluated by commercially available enzyme linked immunosorbent assay (ELISA) kits.

Statistical Analysis: Data processed through independent student t-test by using SPSS version 17. P-value less than 0.05 was considered statistically significant for comparison of control and schizophrenic groups.

RESULTS

In case of thyroid hormones, the levels of T3 (6.9±1.31) and T4 (61.2±15.44) were raised in schizophrenics while TSH (0.28±0.10) was decreased as compared to control group (1.1±0.31; 48.2±10.0 and 1.5±0.32) respectively and were statistically significant (P<0.05).

Table No, 1: Serum circulating biomarkers of schizophrenicsand controls

Parameters	Control (n=25)	Schizophrenics (n=75)	P-value (<0.05)
ALT	24.00±5.69	31.75±19.73	.028
AST	20.25±5.21	29.50±9.32	.011
ALP	55.83±6.28	169.16±13.53	.023
TB	1.01±0.07	1.89±0.02	.041
TCh	4.44±0.37	5.60±0.41	.004
Tg	1.24±0.15	1.81±0.11	.030
LDL	2.31±0.15	3.18±0.52	.005
HDL	1.73±0.17	1.18±0.04	.001
SOD	0.73±0.025	0.06±0.05	.016
GSH	9.77±1.17	7.24±0.94	.005
Catalase	4.27±0.73	2.77±0.83	.033
MDA	3.71±0.91	7.8±2.71	0.03
Ca^{++}	12.03±3.26	13.34±3.67	.036
Na^{+}	143.15±8.26	177.78±2.88	.013
K^{+}	5.07±1.02	1.99±0.03	.000
Mg++	3.45±0.18	1.89±.54	.058
TSH	1.5±0.32	0.28±0.10	0.032
T3	1.1±0.31	6.9±1.31	0.021
T4	48.2±10.0	61.2±15.44	0.04

P value <0.05 (significant)

ALT=IU/L, AST=IU/L, ALP=IU/L, TB (Total Bilirubin)=mg/dl, TCh (Total cholesterol)=mg/dl, Tg (Triglycerides)=mg/dl, LDL=mg/dl, HDL=mg/dl, MDA=nM/ml, SOD=ng/ml, GSH=mg/dl, CAT=µM/mol of protein, Na^{+}=132-142 mEq/L, K^{+}=4.0 - 4.7 mEq/L, Ca^{++}=9-11 mEq/L, Mg^{++}=1.8-3 mg/dL, TSH=mIU/L, T3=ng/ml, T4=nmol/L

From the results presented in Table-01 shows that all the tested circulating biochemical markers e.g. alnine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin exhibited highly significant (P=.05, .028, .011, .023 and .041 respectively) differences not only between the study groups but also between within the same group. The highest values of ALT (31.75 IU/L), AST (29.50 IU/L and TB (1.89 mg/dl) were recorded in schizophrenics patients respectively.

The results depicted in Table-01reflecting that the lipid profile (TCh, Tg, LDL and HDL) of schizophrenics patients versus control differed significantly (P=.05, .044, .030, .007 and .001 respectively). An increasing trend of TCh (5.60 and 5.18 mmol/L), Tg (1.81 and 1.85 mmol/L) and LDL (3.18 and 4.88 mmol/L) was observed both in schizophrenics patients versus control but a decreasing trend of HDL was recorded in both the studied groups (1.18 and 1.22 mmol/L) respectively.

Data in Table-01regarding stress biochemical markers SOD (Superoxide dismutase), GSH (Glutathione) and CAT (Catalase) shows highly significant pattern between and within the studied groups. The consistent decreasing trends in case of Glutathione from groups A-B were recorded (9.77, 7.24 and 5.04 µg/dl) respectively. Catalase levels were also shows the consistent decreasing trend (4.27, 2.77, and 3.74 µmol/mol of protein) in different studied groups (A-B). The lowest value (0.06 ng/ml) of SOD was recorded in group B (Schizophrenicspatients) as compared to control (0.73 ng/ml). Data depicted Table-01regarding electrolytes profile of schizophrenics verses control shows highly significant differences between and within the studied groups.

DISCUSSION

Nearly 1% of the world population has been suffering from schizophrenia (Ong et al., 2010). Investigations have revealed that reactive oxygen species (ROS) are the major role player in pathogenesis of schizophrenia along with the alleviation in enzymatic and non-enzymatic anti-oxidants in the biological system. Particularly, hydrogen peroxide (H_2O_2) has been found to be an important component of the thyrocytes, in normal physiological conditions, for the oxidation of iodide into iodine accomplished by thyroperoxidase [7](De Deken et al., 2002; [8]Schweizer et al., 2008). Higher level of oxidative stress has been observed by the increase of MDA (7.80±2.71) in the patients suffering from schizophrenia as compared to control (3.71±0.91) group. Results of oxidative stress are in agreement with [9] Chittiprolet al., (2010) and Akiibinu et al., (2012). The levels of MDA were decreased after the treatment in schizophrenic patients (Chittiprol et al., 2010).

As far as anti-oxidative system is concerned, various enzymatic and non-enzymatic anti-oxidants are involved for the maintenance of normal physiology of biological system. The levels of anti-oxidants are altered in pathological state as in case of schizophrenia

[10](Gama et al., 2006; [11]Dadheech et al., 2008; [12]Padurariu et al., 2010). Most contrasting investigations have been reported in case of schizophrenia as compared to other psychiatric disorders. In current study, the levels of anti-oxidants (enzymatic and non-enzymatic) including SOD, GSH and catalase were decreased in patients as compared to control group (Table-01). Previous investigations elaborate different findings about anti-oxidant levels in schizophrenics. Increased activities of SOD and lipid peroxidation were reported by various investigators (Gama et al., 2006; [13]Kunz et al., 2008; Padurariu et al., 2010). In case of catalase, the results of current study are not in agreement with the previous one. [14]Miljevic et al., (2010) reported no significant change in schizophrenic when treated with clozapine.

Schizophrenia could be explained on the basis of electrolytes like sodium, potassium, calcium and magnesium. The alterations and/or imbalance were observed in the patients suffering from schizophrenia. The raised levels of sodium (177.78±2.88) and calcium (13.34±3.67) were observed while decreased levels of potassium (1.99±0.03) and magnesium (1.89±0.54) were found in patients as compared to control group (Table-01). The results of current study are contradicted with the previous studies conducted by [15](Sethi and Sethi) (1971) and [16](Bhatia et al., (1987) in case of potassium and magnesium. According to their findings the levels of these two electrolytes were increased in patients. On the other hand, raised levels of sodium and calcium are in agreement with the previous findings of Bhatia et al., (1987), [17](Hoagland (1955) as well as [18]Alexander et al., (1978).

In case of thyroid hormones, the levels of T3 and T4 were raised in schizophrenics while TSH was decreased as compared to control group and were statistically significant ($P<0.05$). The results of thyroid hormones are in agreement with Akiibinu et al., 2012. According to the previous findings the levels of thyroid hormones (total T3 and free T3) were significantly raised in schizophrenics [19](Yazici et al., 2011). MDA was significantly correlated with T3 in patients suffering from schizophrenia (Akiibinu et al., 2012).

CONCLUSION

All the circulating biochemical markers were statistically significant ($P<0.05$). It is concluded that lipid peroxidation may has association with thyroid hormones and electrolytes. Moreover, alleviated concentration of anti-oxidant biomarkers like SOD, catalase and GSH may play a central role in schizophrenics and anti-oxidant therapy may be useful for the management of this psychiatric disorder.

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Original Article

Disorders of the Musculoskeletal System amongst Practicing Dentists

Disorders of Muscles in Dentists

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ABSTRACT

Objective: The aim of this study is to find out the frequency of musculoskeletal disorders among dentists working in Karachi and to establish factors associated with these disorders.

Study Design: Cross-sectional descriptive and analytical study

Place and Duration of Study: This study was conducted at Jinnah Medical and Dental College, Karachi from June 2014 to August 2014. The data was collected from three dental colleges of Karachi.

Material and Methods: The study was conducted at Jinnah Medical and Dental College. The study included 222 dentists working in different faculty positions from house officers to professors. The data was collected to find out the frequency of musculoskeletal disorders among dentists working in five different dental institutions of Karachi. A 22-item questionnaire was used to collect the data. The questionnaire was validated among a group of five dentists before using it for final survey. The questionnaire consisted of number of questions about age, gender, number of years in profession, pain in the back and neck, working hours per day, number of patients treated per day, any break taken between patients or not, working with assistant or not, working positions used, and medicines taken due to musculoskeletal pain. The data was stored in excel worksheet and was analyzed using SPSS.

Results: 222 dentists from five dental institutions of Karachi participated in the study. The study sample comprised of 90 males (40.5%) and 132 females (59.5%). The study highlighted that dentist who are involved in clinical practice are more prone to musculoskeletal problems accounting for about 79%. Amongst these 52.8% having backache, while 43.9% of the dentists having pain in the neck. The factors that were found to be significantly associated with musculoskeletal pain included; Dentists working without assistance experience more musculoskeletal problem approximately 47.6%. Dentist working more than 7 hours a day experienced more neck pain 40%.

Conclusion: In the light of this study it is apparent that musculoskeletal disorders are very common amongst the dentist working in Karachi. It is seen more in those who are working for long hours and those working without trained assistants. Breaks between patients and reducing the number of working hours as well as trained dental assistance can reduce the incidence of these disorders.

Key Words: Dentist, Musculoskeletal disorders, Back and Neck pain

INTRODUCTION

The dental practice is challenging, the deleterious effects of work environmental affect the physical health of the dentists[1,2,3].

Studies suggest that dentists are more vulnerable to certain disorders especially musculoskeletal disorders and in most cases these disorders are profession-related[4,5].

Musculoskeletal pain has become a significant issue among dental professionals, as they often assume static positions that are uncomfortable, asymmetric and for long intervals. In dentistry, improper working habits, inconvenient posture as well as repetitive tasks, such as: root canal instrumentation, cavity preparation and filling, scaling or root planning, contribute greatly to musculoskeletal disorders[6,7].

Approximately 81% of American dentists suffer from neck, shoulder and lower back pain[8]. Similar results were reported by Kerosuo et al.[9] who discovered that 70% of surveyed Scandinavian general dental practitioners and 72% of orthodontists experienced musculoskeletal symptoms.

In Pakistan, a study in Peshawar says that almost 56% of dentists experienced backache and 41% had pain in the neck[10]

The aim of this study is to find out the frequency of musculoskeletal disorders among dentists working in Karachi and to establish factors associated with these disorders.

MATERIALS AND METHODS

The cross-sectional descriptive and analytical study was conducted at Jinnah Medical and Dental College. The study included 222 dentists working in different faculty positions from house officers to professors. The data was collected to find out the frequency of musculoskeletal disorders among dentists working in five different dental institutions of Karachi. A 22-item questionnaire was used to collect the data. The questionnaire was validated among a group of five dentists before using it for final survey. The

questionnaire was designed to take approximately five minutes to complete. The questionnaire consisted of number of questions about age, gender, number of years in profession, pain in the back and neck, working hours per day, number of patients treated per day, any break taken between patients or not, working with assistant or not, working positions used, and medicines taken due to musculoskeletal pain.

The data was stored in excel worksheet and was analyzed using SPSS.

RESULTS

222 dentists from five dental institutions of Karachi participated in the study.

The study sample comprised of 90 males (40.5%) and 132 females (59.5%). On the basis of age the study sample was divided in three groups; group 1= 25-34 years, group 2 =35-44 years and group 3 = 45-54 years. There were 196 (88.2%) dentists in group 1, 23 (10.2 %) in group 2 and only 3 (1.6 %) in group 3. The clinical experience was also divided into three groups 1-5 years, 6-10 years and more than 10 years. There were 72 % practitioners in 1-5 years group, 10% in 6-10 year group and 18 % had more than 10 years of clinical experience.

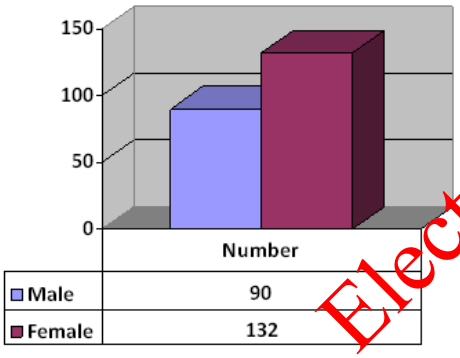

Chart No.1: %age of male & female patients

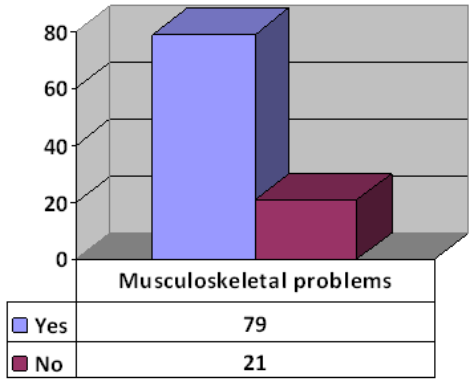

Chart No.2: %age of musculoskeletal problems

The study highlighted that dentist who are involved in clinical practice are more prone to musculoskeletal problems accounting for about 79%. Amongst these 52.8% having backache, while 43.9% of the dentists having pain in the neck. Some had issues in multiple regions simultaneously that included neck and shoulder 5%, neck shoulder and lower back 13%, neck wrist and lower back 8%, knee and lower back 2%, knee wrist shoulder and elbow 2%, 2% all over symptomatic and 17% had no symptoms.

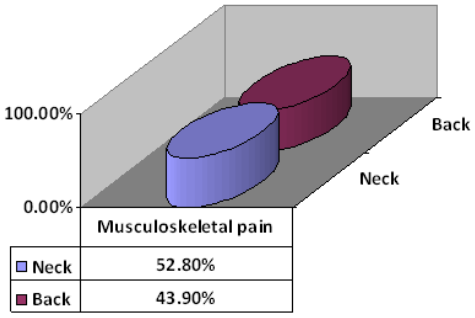

Chart No.3: %age of musculoskeletal pain in patients

The factors that were found to be significantly associated with musculoskeletal pain included; Dentists working without assistance experience more musculoskeletal problem approximately 47.6%. Dentist working more than 7 hours a day experienced more neck pain 40%. Breaks between patients, was insignificant and was not associated with any musculoskeletal problems in this study. The relationship of musculoskeletal disorder and the right or left hand dominance was insignificant in the study.

DISCUSSION

In this study a questionnaire was used to determine the prevalence of musculoskeletal disorders amongst the practicing dentists in the seven dental institutions of Karachi. The purpose was to identify the relationship between musculoskeletal disorder and working time, working with or without assistant, breaks between patients and posture.

It is the first effort of its kind done in Karachi to determine the reasons for musculoskeletal pain among dental professionals in Karachi. A total of 222 dentists working in different faculty positions from house officers to professor level participated in the study.

Our study showed that 79% of dentists experienced musculoskeletal pain. The result is comparable to a similar study conducted in Peshawar in 2012 which showed[10]. The high percentage of dentist showing sign of musculoskeletal pain is alarming. In literature the frequency for the dentist having back pain ranges from 35-55%[6,7,8].

Our study highlighted that amongst the dentist having musculoskeletal pain 52.8% having backache, while 43.9% of the dentists having pain in the neck. Interestingly some had issues in multiple regions simultaneously that included neck and shoulder 5%, neck shoulder and lower back 13%, neck wrist and lower back 8%, knee and lower back 2%, knee wrist

shoulder and elbow 2%, 2% all over symptomatic and 17% had no symptoms

The results of our study found that there is directly proportional effect of the number of working hours to the development of musculoskeletal pain. The study suggests that 40% of the dentist working for are more than 7 hours per day had back or neck pain.

Working without a dental assistant can also lead to musculoskeletal disorders. In this study 47.6% of the dentist working without assistant had back, neck or combination pain. Our results also indicate that the complaints of back pain were strongly related to the number of patients treated daily.

These results show that the musculoskeletal disorders are seen more in dentist working for long hours and those working without assistance. We recommend that the dentist should either reduce the working hours or take long breaks between patients and should work with properly trained dental assistants to avoid or at least reduce the incidence of musculoskeletal disorders.

CONCLUSION

In the light of this study it is apparent that musculoskeletal disorders are very common amongst the dentist working in Karachi. It is seen more in those who are working for long hours and those working without trained assistants. Breaks between patients and reducing the number of working hours as well as trained dental assistance can reduce the incidence of these disorders.

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Original Article

Infection Control Protocols

Practice of Universal Infection Control Protocols

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ABSTRACT

Objective: The objective of this study was to evaluate practice of universal infection control protocols among third and final year BDS students at different dental colleges.

Study Design: Comparative study

Place and Duration of Study: This study was conducted in five dental colleges and hospitals which are affiliated with University of Karachi during the year 2011-2012.

Materials and Methods: The undergraduates (third and final professional BDS students were selected with the age range from 18-22 years and without gender discrimination in the year 2011-2012. A self applied, confidential 14 close-ended type questionnaire consisting of various aspects of infection control practice was distributed to these undergraduates at the end of second semester after the lecture with permission and consent of head of institution. The collected data was analyzed by using SPPS 16.0.

Results: Among 180 students, 90(50%) were final year students and 90(50%) were third year students. Out of them 70 final year and 72 third year students participated. Thus a total of 142 (77.77%) students completed questionnaire with a response rate of 79%. The final year students were found to have more knowledge and had practiced more infection control procedures than third year students.

Conclusion: Compliance with recommended guidelines for cross infection control varies among final year and third year students. Efforts are needed to improve attitudes to implement information and motivate students in the correct and routine use of infection control measures before they commence their clinical rotations.

Key words: risk of infections, sterilization, third year, final year, infection control procedures.

INTRODUCTION

Dentists, dental students, patients, assistants and technicians are exposed to pathogenic microorganism during dental treatment. Microorganisms can be transmitted from dentist to patients and patients to patients through direct or indirect contact with contaminated objects (blood, fluids, instruments, and surfaces) and secretions from conjunctiva, nose and oral cavity[1].

The carriers of microbial diseases are not easy to identify therefore "Centre for disease control" (CDC) recommended universal precautions regarding infection control in dentistry to reduce risk of infections among dentists, assistants, technicians, students and patients[2-7]. The term "Universal Precautions" (modified into "Standard Precaution" in 1996 by CDC) were applied to contact with contaminated blood, body fluids secretions, non broken skin and mucosa, droplets during treatment should be considered as infectious[8]. In different dental schools the overall reported occurrence rates for "needle stick and sharp injuries" (NSIs) have ranged from 1.97/10,000 visits to 12.5/10,000 visits[9]. Younai et al mentioned the higher frequency of injury for third-year students compared to fourth-year students suggesting an elevated risk among the third year students due to inexperience and improper handling during performing invasive procedures[10].The majority of dental residents experienced NSIs those occurred extra-orally during removable prosthetic procedures[9].

Dental surgeons and staff are more prone to Hepatitis and Human Immunodeficiency Virus (HIV) infections[7]. Researchers have proved that the chances of hepatitis B infection after needle stick injuries are more compared to HIV infections[11]. Exposure to infectious agents are accidental in the dental practice and following infection control guiding principle can decrease the chances of cross infection. Sometimes it is very difficult to prevent the exposure, but the correct management after exposure and immunization can be helpful to reduce the chance of cross infection and maintain the defense system[12]. Al-Sohaibani et al. recommended vaccination against HBV to all physicians of Saudi Arab due to their high occupational risk of HBV infection[13]. The compliance of dentists with these specific recommendations and infection control programs has also been studied in many countries[14,15].

There was a lack of local data on this topic therefore study was designed to evaluate the practice of universal infection control protocols among dental students at different dental colleges and universities.

Inclusion Criteria;

- Students of 3rd BDS (juniors) and 4th year BDS (seniors)
- Both genders with age range from 18-22 years.
- Completely filled questionnaire.

Exclusion Criteria;

- First and second year BDS students
- House officers and Post Graduates trainees

MATERIALS AND METHODS

This study was conducted in five dental colleges and hospitals which are affiliated with University of Karachi. It is an observational study in which 180 samples (90 final year and 90 third year students) are drawn through a non-randomized, purposive sampling procedure. A self applied questionnaire containing 14 close-ended questions related to infection control knowledge and practices were distributed among final and third year dental students. The Statistical Package for the Social Sciences (SPSS) version 16.0 was used for the calculations. Results were analyzed and compared by means of frequency and associated statistical tests.

RESULTS

Out of 180 students included 90 were fourth year and 90 were third year students. Only 70 from fourth year and 72 from third year completed the questionnaire. Thus a total of 142(79%) students completed questionnaire.

Out of these 142 students, variation was observed in their count with respect to different infection control regimes being practiced. 72 students (50.7%) (41 final year and 31 third year) informed that they take medical history. 110 students (75%) (62 final year and 48 third year) were immunized against hepatitis B and C. 132 students (96.4%) (68 final year and 64 third year) wore gloves for every dental procedure. 138 (97.9%) (74 final year and 64 third year) informed that they change gloves after each patient. 120 (85.3%) (65 final year and 55 third year) wore face mask. 26 students (18.3%) (15 final year and 11 third year) replaced face mask after every dental procedure (table 1).

A total of 115 students (81.7%) (65 final year and 50 third year) changed extraction instruments after each patient. Only 33 students (23.3%) (20 final year and 13 third year) knew the importance of changing hand piece. 118 students (83.5%) (60 final year and 58 third year) were particular about changing saliva ejectors and only 69 students (48.6%) (49 final year and 20 third year) were educated in regard to the use of sterilized burs between patients (table 1).

However only 39 students (27.46%) (29 final year and 10 third year) used autoclave for sterilization. Plastic wrapping for sterilization of instruments were used by 24 students (16.9%) (16 final year and 8 third year). Rubber dam was used by 22 final year students only (15.8%) while 58 students (44.8%) (38 final year and 20 third year) reported the use of special containers for disposal of sharp objects (table 1).

Table No.1: Comparison of final year and third year students

S. No.	Question	Response Yes			Response No	Total participants
		Final year	Third year	Total	Total	
1.	Medical History	41(56.9%)	31 (43%)	72 (50.7%)	70 (49.3%)	142
2.	Vaccination for hepatitis B and C	62(56.3%)	38(34.5%)	110 (75.2%)	32 (24.8%)	142
3.	Wearing of Gloves	68(51.5%)	64(48.4%)	132 (96%)	10 (5.6%)	142
4.	Changing gloves after each patient	74(53.6%)	64(46.3%)	138 (97.9%)	4 (10%)	142
5.	Wearing Of Face mask	65(54.1%)	55(45.8%)	120 (85.3%)	22(14.7%)	142
6.	Face mask changing between patients	15(57.6%)	11(42.3%)	26 (18.3%)	116 (81.7%)	142
7.	Changing extraction instruments	65(56.5%)	50 43.4%)	115 (81.7%)	27 (18.3%)	142
8.	Changing hand pieces	20(60.6%)	13(39.3%)	33 (23.3%)	109 (76.7%)	142
9.	Changing saliva ejectors	60 50.8%)	58(49.1%)	118(83.5%)	24 (16.5%)	142
10.	Changing burs	49 (71%)	20 28.9%)	69(48.6%)	73 (51.40%)	142
11.	Use of autoclave for sterilization of instruments	29(74.3%)	10 25.6%)	39 (27.46%)	103 (72.5%)	142
12.	Use of plastic wrappings for sterilization of instruments	16(66.6%)	8 (33.3%)	24 (16.9%)	118 (83.1%)	142
13.	Use of rubber dam	22 (100%)	0	22 (15.8%)	120 (84.8%)	142
14.	Disposal of sharp objects	38(65.5%)	20(34.4%)	58 (44.8%)	84 (59.2%)	142

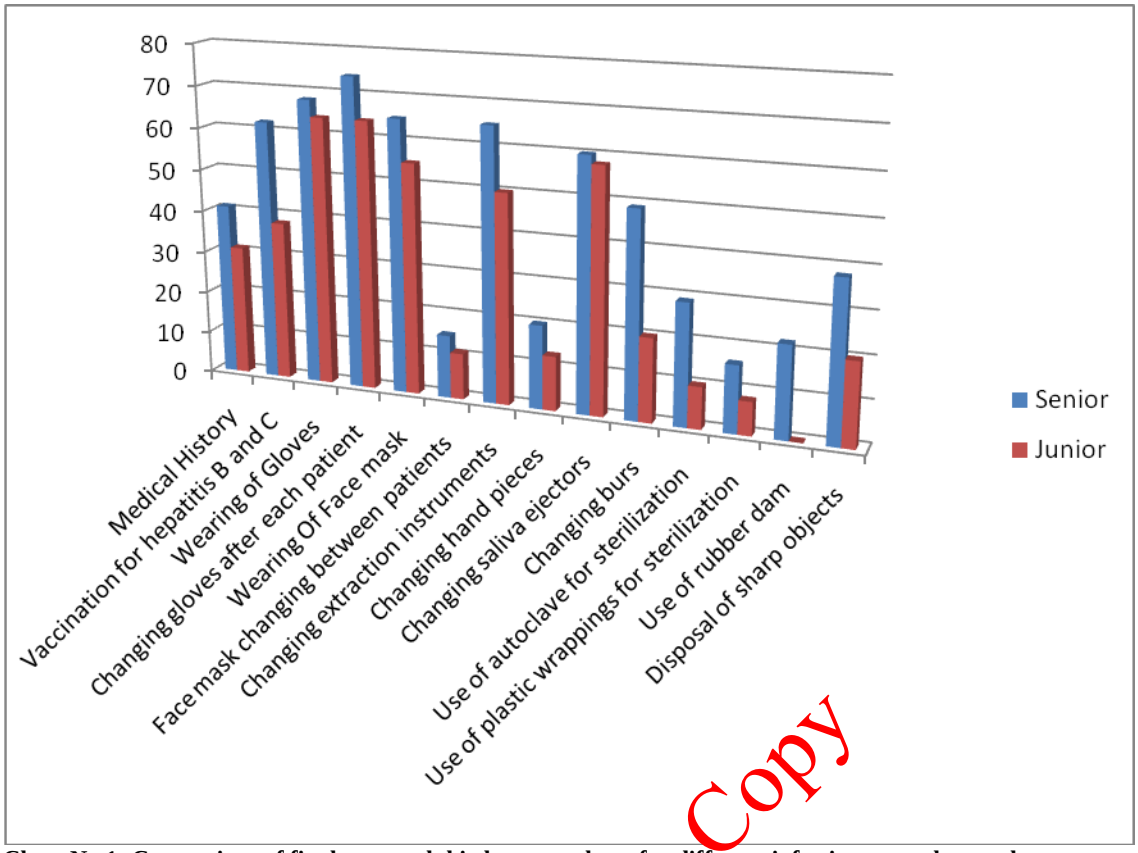

Chart No.1: Comparison of final year and third year students for different infection control procedures

DISCUSSION

Many researchers have revealed that the chances of hepatitis B and C infections were high among dental professionals after needle stick exposure in their studies[16]. Thus, vaccination for hepatitis B coverage was suggested for all dental health care professionals[17]. Rahman et al[18] revealed that 95.8% of final year students were vaccinated against Hepatitis B[18]. However McCarthy and Britton[12] showed 100% immunization in final year students in comparison to our study in which 110 (75.2%) dental students were vaccinated against hepatitis B. The vaccine is cost effective and easily available, thus vaccination of dental health care professionals can be achieved in low cost[19].

Many microorganisms including viral, fungal and protozoa are harmful for dental surgeons and patients. They are more prone to exposure to these microbes either direct contact with blood, skin, and saliva of patient or by indirect contact by sharp instruments or from aerosols[20]. Dental professionals must wear gloves and mask in order to prevent the transmission of source of infection and reduce the risk of infection from operators to the patients and from patients to operators[21]. Rahman et al[18] stated that in his study 99.2% of final year students wore gloves while 98.3% wore face masks as compared to our study in which 133 (96.4%) dental students wore gloves and 120 (85.3%) facemasks. Kumar et al[22] reported that in his study only 21.7% of final year students and 1.4% of third year students changed face masks after each patient which is in high contradiction to our study in which 57.6% of final year and 42.3% of third year students did the same.

The vulnerability of cross infection with the use of dental instruments was emphasized by many authors[23,24]. In order to protect the instruments from environmental contamination, the instruments are packed in proper wrapping material before sterilization[25]. Kumar et al[22] reported that only 11.6% of final year and only 8.3% of third year students used plastic wrapping before the sterilization of instruments in comparison to our study in which 66.6% and 33.3% respectively did the identical practice. In another study by Singh et al[26] 94.3% of undergraduates used autoclave for sterilization as compared to our study in which only 27.46% used autoclaves.

All sharp objects should be disposed of properly in safe, punctured proof containers[27,28]. In the present study, about 44.8% of dental students used containers for sharp instruments which is in accordance with previous study[19] and Kumar et al[22].

Several studies reported that contamination of dental clinics can be reduced by using high-volume suction[7,29,30]. Kumar et al[22] reported that 56.5% of final year students changed saliva ejectors which is in

accordance to our study which is 50.8% but a significant difference when compared to third year students which is 81.9% and 49.1% respectively.

Ryan et al[31] stated that in his study rubber dam was used by 98.5% of undergraduates as to prevent cross infection which is in contradiction to our study and Al Kholani[32] which is only 15.8% and 3.9% correspondingly (table 1). This vast difference could be because of lack of knowledge on the importance of using rubber dam.

Changing burs and extraction instruments between patients was practiced by 88% and 85% respectively by undergraduates in a study of Al-Kholani[32] and in this study it was implemented by 48.6% and 81.7% students respectively.

A study showed that dentists with ten or more years of experience were significantly more familiar with infection control procedures than the undergraduate students of dentistry[33]. Another study explained that dental professionals above 40 years of age were more prone to utilize specific infection control methods than the dentists who were below 40 years[34]. The data in the study were self reported, and it is important to be vigilant in interpretation of results. In this study we also observe that senior students were significantly familiar enough with infection control procedures.

CONCLUSION

Our observations indicate a lack of understanding of the basics of infection control and the prevention of transmission of communicable infectious diseases. However final year students display more protocol in regard to infection control regime as compared to third year students.

Recommendations: It is necessary to effectively communicate to students the associated risks and importance of transmission of infectious diseases and exposures during dental treatments. Efforts are needed to improve attitudes to implement information and motivate students in the correct and routine use of infection control measures. With all infection control protocols already implemented in dental schools the challenge remains on improving compliance with infection control recommendations. In addition courses and workshops on infection control techniques should be conducted in order to implement knowledge into practice.

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Original Article

HCV

Significance of Hepatic Profile and Malondialdehyde as Marker of Lipid Peroxidation in HCV Patients: A Perspective Study from Local Population of Punjab

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ABSTRACT

Objective: All over the world Hepatitis C virus (HCV) remains to be a main etiological mediator of liver disease. Approximately, 10 million people in Pakistan are diseased with HCV. Pegylated interferon plus ribavirin signifies the gold standard therapy but various side effects may occur.

Study Design: Comparative study.

Place and Duration of Study: This study was conducted at Jinnah Hospital Lahore from August 2013 to March, 2014.

Materials and Methods: Thirty five patients of hepatitis C virus and Twenty three age and sex-matched clinically apparently healthy individuals were eligible for inclusion in the study at Jinnah Hospital Lahore during the year 2013-2014. 1.0 ml blood sample were taken and subjected to centrifuge at 3000-4000 rpm for 10-15 minutes for the separation of serum. All the analytical work was performed at the Institute of molecular biology and biotechnology (IMBB), and Centre for research in molecular medicine (CRiMM), The University of Lahore-Pakistan.

Results: The estimation of AST, ALT, ALP, TP and T.Bilirubin were estimated. The AST level in HCV patients was increases (47.88±40.49) as compared to the control persons (31.43±7.31) and statistically significant (0.02<0.05). Total Protein level in HCV patients was (4.20±0.61) and in healthy individuals (6.23±0.51) and statistically significant (0.000<0.05). MDA level in HCV patients was increases remarkably (8.58±1.19) and in control persons (1.47±0.54) and it was statistically significant (0.000<0.05).

Conclusion: There is a relationship between oxidative stress and ALP, ALT, AST and Albumin. The results of the present study confirmed a perfect sketch regarding the circulating biochemical markers and lipid peroxidation (MDA) profile between the studied groups i.e., control and HCV patients with interferon induced Hepatitis C virus infection.

Key Words: MDA, ALT, AST, ALP, HCV, Interferon.

INTRODUCTION

Hepatitis C virus (HCV) is the main mediator of liver diseases in all over the world. HCV virus is mainly transferred during surgical operations i.e. replacement of organs, blood transfusions or by using contaminated syringes. This virus belongs to the gene Hepacivirus and it is RNA virus (Ogata et al., 1991; Simmonds et al., 1994)[1,2]. There are six main types of HCV genotypes (Kuiken and Simmonds, 2009)[3]. Out of six, genotype 2, 3, 5 and 6 were reported frequently (Al-Faleh et al., 1995; Osaba et al., 2000; Karkar, 2007; Alzahrani et al., 2009)[4,5,6,7]. Those people which receive organs, blood or blood products from those people which were already affected by the HCV-virus have a greater risk of this infection (Alter et al., 1989; Esteban et al., 1990; Vander et al., 1990)[8,9,10]. Liver cirrhosis and hepatocellular carcinoma (HCC) are caused by the chronic HCV (Seeff et al., 1992; Kaneko et al., 1994)[11,12]. A person with strong immune system has the ability to boost the HCV allowance (Cooper et al., 1999; Rehermann and Nascimbeni, 2005)[13,14]. It is estimated that approximately 10 million people are affected by HCV in pakistan.3a followed by 3b and 1a is the most dominant genotype in Pakistan (Ahmad et al., 2010)[15].

As genotype 3a largely exist in Pakistan due to which HCV genotyping is not suggested for patients infected by HCV by Gastroenterology Society of Pakistan (Hamid et al., 2003).[16] Secondly due to inadequate facilities and the expense on genotyping test, most patients deprived of genotyping test. But on the contrary, genotyping gives information about strain variation, potential association with severity of the disease and treatment response (Derbula et al., 2006; Kabir et al., 2006)[17,18]. Pegylated interferon and ribavirin proves a valuable therapy for Hepatitis C virus (HCV) but also has some side effects (Dusheiko, 1997;

Negro, 2010)[19,20]. Some adverse effects are also reported which may lead to life-threatening results. In the patients, liver fibrosis, cirrhosis and hepatocellular carcinoma (HCC) are the major causes of HCV (Giannini and Brechot, 2003)[21]. From last few years, scientists strived to compare viral and biochemical factors including ALT, AST, bilirubin, genotype with each other and liver damage but no inference was formulated (El-Serag, 2002; Skehel, 1992; Kato and Eggers, 1969; Pratt and Kaplan, 2000)[22,23,24,25].

MATERIALS AND METHODS

Source of Data:

I. Thirty five patients of hepatitis C virus were eligible for inclusion in the study at Jinnah Hospital Lahore during the year 2013-2014. Detailed history, clinical complications, habits in particular smoking and tobacco chewing were collected from subjects of the study by giving them a questionnaire. Clinical diagnosis of the patient was also taken into consideration.

II. Twenty three age and sex-matched clinically apparently healthy individuals were included as controls.

III. All the analytical work was performed at the Institute of molecular biology and biotechnology (IMBB), and Centre for research in molecular medicine (CRiMM), The University of Lahore-Pakistan.

Method of Collection of Data: Blood samples were collected with aseptic precaution. Informed consent from subjects was obtained before collection of blood samples.

Sample and Sampling Technique: Blood samples of Patients and controls were collected and processed. 5ml blood was collected in EDTA-Vaccutainers and centrifuged.

Chemicals: All chemical reagents of analytical grades were purchased from Sigma Chemical Co. (St. Louis, Mo, USA).

Following Parameters were Estimated:

Biochemical Assays for Liver Function Tests: Blood sample were taken and subjected to centrifuge at 3000-4000 rpm for 10-15 minutes for the separation of serum. The estimation of AST, ALT, ALP, TP and T.Bilirubin were estimated by using commercially available Bio Merux and Randox kits. Malondialdehyde (MDA) was estimated by Ohkawa et al., (1979)[26] method.

RESULTS

The data presented in table: 1 is the clear cut picture of the different parameters estimated in HCV patients. It was observed that the level of ALT in HCV patients was (40.51) as compared to the healthy individuals (32.78) but observed that it was statistically non-significant. The AST level in HCV patients was elevated remarkably (47.88) as compared to the control persons (31.43) and it was statistically significant (0.02<0.05). When the ALP level was estimated, it was observed that ALP level was increased in HCV patients (202) while in healthy individuals it was (84). Total Protein level in HCV patients was (4.20) as compared to controls (6.23). It shows that total protein level was decreased in HCV patients and was statistically significant (0.000<0.05). Total bilirubin level in HCV patients was observed (0.95) while in healthy individuals it was (0.88). When the Albumin was observed in patients it was found that albumin level was decreased in HCV patients (3.10) as compared to the control (4.12) and also found that it was statistically significant (0.000<0.05). MDA level was increased remarkably (8.58) as compared to the healthy individuals (1.47) and it was statistically significant (0.000<0.05).

Table No.1: Comparison of different parameters in HCV patients and control

Variables	Control (n=23)	HCV Patients (n=35)	(P < 0.05)
Age	33.04±6.63	40.94±11.53	0.002
ALT	32.78±20.46	40.51±41.69	0.413
AST	31.43±7.31	47.88±40.49	0.024
ALP	84±7.10	202±76.26	0.375
Total Protein (TP)	6.23±0.51	4.20±0.61	0.000
Total Bilirubin (T.Bili)	0.88±0.27	0.95±0.46	0.492
Albumin (ALB)	4.12±0.48	3.10±0.21	0.000
Malondialdehyde (MDA)	1.47±0.54	8.58±1.19	0.000

Table No.2: Comparison of different parameters between genders of HCV patients

Variables	Males (n=28)	Females (n=30)	(P <0.05)
Age	35.71±10.36	39.76±10.53	0.146
ALT	38.75±40.25	36.23±29.54	0.786
AST	40.82±30.14	41.86±35.30	0.094
ALP	192±71.16	198±77.85	0.756
Total Protein (TP)	5.26±1.17	4.78±1.09	0.114
Total Bilirubin (T.Bili)	0.94±0.32	0.91±0.46	0.782
Albumin (ALB)	3.54±0.57	3.47±0.64	0.627
Malondialdehyde (MDA)	5.05±3.86	6.43±3.36	0.154

ALT: IU/L; AST: IU/L; ALP: IU/L; TP: mg/dL; ALB: mg/dL; MDA: nmol/mL

Table No.3: Spearman's correlation coefficients of different variable

Age Vs TOTAL BILIRUBIN (r= -0.474**)
ALT Vs TOTAL BILIRUBIN (r= 0.362*)
AST Vs TOTAL PROTEIN (r= -0.359**)

The data presented in table 2 shows the comparison between males and females suffering from HCV. 28 HCV infected males and 30 female patients were taken. The ALT level in males was observed (38.75) while in females it was (36.25). Data showed that the AST level in males was (40.82) and in females was (41.86). When ALP level was measured in Males and it was found to be (192) as compared to females (198). Total protein level in males was (5.26) and in females (4.78). When MDA level was observed in males it was found to be (5.05) while in females patients it was (6.43). Data also showed that all the parameters are statistically non-significant (P>0.05) and also observed that in the progression of disease, gender does not matter.

Table 3 shows the correlation exists between different parameters. Data showed that inverse correlation exists between AGE and total bilirubin (r = -0.474**). It means that with the increase of AGE the amount of total Bilirubin decreases. Positive correlation was found between ALT and Total Bilirubin (r = 0.362*). Negative correlation was found between AST and Total Protein level (r = -0.359*).

DISCUSSION

Hepatitis C virus (HCV) is a RNA virus which has been known to cause acute and chronic necroinflamatory disease of the liver. It infects more than 170 million people worldwide. In Western countries, HCV is the leading cause of end-stage liver disease and hepatocellular carcinoma, as well as the main indication for liver transplantation (Kuiken and Simmonds, 2009; Khattab et al., 2011)[3, 27]. In more than 70% of the infected people, the disease becomes chronic and leads to chronic hepatitis, 5-20% develops cirrhosis, and 1-5% died from cirrhosis or liver cancer. Furthermore, use of contaminated syringes, drug abuse, and use of barber razor, dental procedures, tattooing, ear piercing, acupuncture and high-risk sexual behavior are other modes of transmission (Grobusch et al., 1999)[28]. The first discovery of Interferon (IFN)-α, a cytokine produced after stimulation of leukocytes or fibroblasts with virus infection or nucleotide treatment, growing numbers of subtypes of IFN have been identified. Of these, IFN- α and IFN- β species have been used in the treatment of hepatitis. IFN therapy is an effective method of clearing the hepatitis C virus (HCV) from serum, normalizing biochemical liver function and improving liver histology in chronic hepatitis C patients. Nevertheless, only about 40 of patients respond to this therapy and up to 60 of responders showed reactivation of the disease after IFN withdrawal (Fried and Hoofnagle, 1995)[29].

The study was assessed to evaluate the different parameter levels in Hepatitis C virus patients ALP, Albumin, ALT, Total protein, AST and oxidative biomarker MDA was measured in acute hepatitis and chronic necroinflamatory disease of the liver patients. Parameters were calculated in these studies on 35 patients and 23 controls. Oxidative stress conditions are categorized with a raise in the concentration of reactive oxygen specie that can cause destruction at different cellular level association (Feron et al., 1991)[30]. Negative correlation exist between age and total bilirubin (r = -0.474**) and this is significant correlation. While there is positive correlation exist between ALT and Total bilirubin (r = 0.362*) and this is significant correlation. Whereas Between AST and Total protein negative correlation (r = -0.359) occur and it is also significant correlation.

CONCLUSION

In this current study it is established that there is a relationship between oxidative stress, ALP, ALT, AST and albumin of Hepatitis C virus patients. Biochemical study of the Hepatits C virus patients receiving interferon showed that oxidative stress and ALP, AST, ALT and Albumin play important key role in the progression of HCV. It was also determined that the Hepatits C virus patients have remarkably high lipid peroxidation due to which the level of MDA was increased. And here also levels of AST and TB were increased in this estimation. The results of the present study confirmed a perfect sketch regarding the circulating biochemical markers and lipid peroxidation (MDA) profile between the studied groups i.e., control and HCV patients with Hepatitis C virus infection receiving interferon.

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Original Article

Prevalence and Morphometry of Arcuate Foramen in Atlas Vertebrae in Pakistanis

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ABSTRACT

Objective: To assess the prevalence and morphometry of arcuate foramen and comparison with native foramen transversarium in atlas vertebrae of Pakistani population.

Study Design: Descriptive / observational study.

Place and Duration of Study: This study was conducted at Anatomy department, Sheikh Zayed Medical College Rahim Yar Khan and Wah Medical College Wah Cantt. during a period of two years from Jan 2012 to Dec. 2013.

Materials and Methods: The study included 150 dried human atlas vertebrae. Prevalance of complete arcuate foramina (CAFs) in atlas vertebrae were noted and its anteroposterior and superoinferior diameters were measured by vernier calipers with accuracy of 0.01 mm. Size and shape of CAFs were compared with native foramina transversaria (NFTs).

Results: Out of 150 atlas vertebrae, 13 (8.66%) showed CAF. The mean anteroposterior diameter of the right CAF was 6.71 mm and that of left was 6.76 mm. The mean superoinferior diameter was 5.07 mm on the right and on left side it was 5.22 mm.

The mean cross-sectional area of CAFs was 26.74 mm^2 and 27.77 mm^2 for the right and left sides respectively. The mean cross-sectional area of the right NFTs was 34.86 mm^2, while the mean area for the left was 35.31 mm^2.

Conclusion: This study provides information on the morphometry of arcuate foramen and ipsilateral native foramina transversaria (NFTs) and their implications. The observation that CAFs are smaller than ipsilateral NFTs suggests that they are an important cause of vertebral artery compression syndromes and needs careful investigations. Knowledge of CAF may help the surgeons undertaking procedures in the C1 region.

Key Words: Complete arcuate foramen, ponticulus posticus, atlas vertebra, native foramen transversarium.

INTRODUCTION

The vertebral artery, as it emerges from the native foramen transversarium of the atlas (C1) vertebra, travels posteriorly and medially behind the lateral mass of the atlas and lies in the neurovascular groove on posterior arch of the atlas. Sometimes bony spurs or outgrowths extend from the lateral mass to the posteromedial margin of the groove and are named as posterior bridges (also called ponticles) which convert the neurovascular groove into a sulcus, incomplete or complete foramen.[1] When present this complete foramen is named as arcuate foramen. The alternate names used for this foramen are Kimmerle's variant/anomaly/deformity, ponticulus posterior (ponticulus posticus) of the atlas, retroarticular canal, foramen retroarticulare superior, canalis vertebralis, retrocondylar vertebral artery ring, postglenoidal bridge, posterior bridge, retroarticular bridge, retroglenoidal bridge and superior retroarticular bridge, foramen arcuale, foramen posterius, foramen retroarticulare, or foramen sagittale.[2]

The arcuate foramen can be associated in producing symptoms which may include migraine, vertigo, diplopia, and neck pain.[3,4] It has even been suggested that ponticulus posticus may contribute to vertebral artery compression, vertebrobasilar insufficiency, or vertebral artery dissection.[5] Over the years, researchers have investigated the unilateral or bilateral occurrence of complete arcuate foramen.[6-9]

The present study was designed to determine the incidence of the arcuate foramen and the morphometric differences between the native foramen transversarium and arcuate foramen of atlas vertebrae in our population. The findings of this study might help to elaborate the correlation between occurrence of the bony bridges or ponticles and vertebral artery entrapment.

MATERIALS AND METHODS

This study is based on the examination of one hundred and fifty dry human atlas vertebrae obtained from the Anatomy department of Sheikh Zayed Medical College, Rahim Yar Khan and Wah Medical College, Wah Cantt, district Rawalpindi.

Measurements of maximum dimensions of the arcuate foramen in both anteroposterior (ventrodorsal or length) and superoinferior (rostrocaudal or height) directions were taken. The anteroposterior and mediolateral (horizontal) diameters of the ipsilateral native foramina transversaria (NFTs) were measured in all the atlas vertebrae. These measurements were taken by using

Vernier calipers (Peacock Co., Tokyo, Japan) sensitive to 0.01 mm.

The cross-sectional area of the arcuate foramen and ipsilateral native foramen transversarium was calculated using the formula for the ellipse[10]:

Area (A) = л x D1 x D2 x 1/4

Where D1 = horizontal length of the foramen.

D2 = vertical length of the foramen and

л (Pi) = 3.142 or 22/7

The data was analyzed using the SPSS software version 15.0.

RESULTS

Complete Arcuate Foramen (CAF): The complete arcuate foramen (CAF) was present in 13 vertebrae out of 150 atlas vertebrae (8.66%). The side of appearance of CAF was right in 6 cases (4%), left in 4 cases (2.66%) and bilateral (Fig.) in 3 cases (2%) (Table-I). When viewed as a group, the side of involvement was right in 46.15%, left in 30.77% and bilateral in 23.08%.

The mean anteroposterior diameter of the right CAF was 6.71 mm. The mean superoinferior diameter was 5.07 mm (Table-2). On the right side, the anteroposterior diameter was significantly larger than the superoinferior (p = 0.002).

On the left side, the mean anteroposterior diameter of CAF was 6.76 mm. The mean superoinferior diameter was 5.22 mm. As on the right side, there was statistically significant difference between the anteroposterior and superoinferior diameters.

Native Foramen Transversarium (NFT): On the right side, the mean anteroposterior diameter of native foramen transversarium (NFT) was 7.47 mm. The mean mediolateral or horizontal diameter was 5.94 mm (Table-II). There was significant difference between the anteroposterior and mediolateral diameters (p=0.003).

The mean anteroposteior diameter on the left NFT was 7.44 mm. The mean mediolateral or horizontal diameter was 6.04 mm. As on the right side, there was also statistically significant difference between the two parameters.

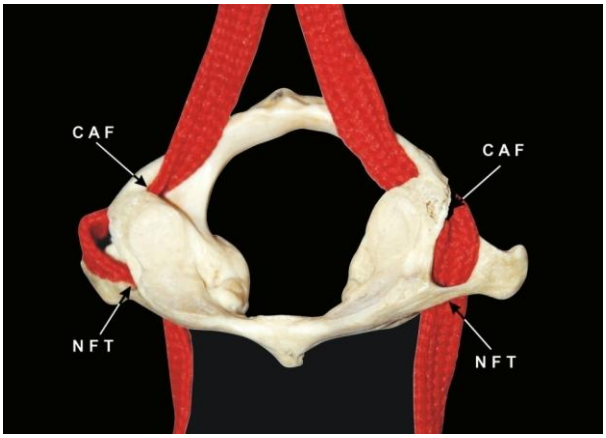

Figure No.1. Photograph of atlas vertebra showing bilateral complete arcuate foramina (CAFs) & native foramina transversaria (NFTs).

Table No.1: Incidence of complete arcuate foramen (CAF) in Pakistani population.

Number of atlas vertebrae studied	Complete Arcuate Foramen (CAF)	Bilateral CAF	Right side CAF	Left side CAF
	n	n	N	n
150	13 (8.66%)	3 (2%)	6 (4%)	4 (2.66%)

Table No.2: The mean diameter and cross sectional area of Complete Arcuate Foramen (CAF) and Native Foramen Transversarium (NFT) present in the atlas vertebrae.

CAF Diameter (mm)				NFT Diameter (mm)				Cross Sectional Area (mm^2)			
Anteroposterior		Superoinferior		Anteroposterior		Mediolateral (Horizontal)		CAF		NFT	
Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
6.71	6.76	5.07	5.22	7.47	7.44	5.94	6.04	26.74	27.77	34.86	35.31

Cross- sectional Area of CAF and NFT: The mean area of complete arcuate foramen (CAF) was 26.74 mm^2 and 27.77 mm^2 for the right and left sides respectively. There was no statistically significant difference in the area on the right and left sides.

The mean area of the right native foramina transversaria (NFTs) was 34.86 mm^2, while the mean area for the left was 35.31 mm^2. There was no statistically significant difference between the two sides.

The mean area of NFT was invariably larger than that of the CAF. On the right side, the statistical significance was 0.05 while on left side it was 0.03.

Ponticle Thickness: There were numerous variations with respect to thickness and configuration of the ponticuli. The mean ponticle thickness was 2.64 mm (1.60 – 3.30 mm).

DISCUSSION

Complete Arcuate Foramen (CAF): The ponticulus posticus is a bony outgrowth over the groove for the vertebral artery located dorsal to the lateral mass on the posterior arch of the atlas vertebra and the foramen formed when complete is called arcuate foramen.

Acurate foramen has been studied in skeletal bones,[11-16] radiographs,[17-22] and CT Scans[23,24] in different populations. In the studies performed on skeletal bones, retroarticular canal of atlas vertebra is classified in three groups. Class-I represents retroarticular impression on the posterior arch of atlas vertebra, Class-II is defined retroarticular sulcus, and Class-III represents complete bony ring or complete arcuate foramen (CAF).

Table No.3: Incidence of complete arcuate foramen in human atlas vertebrae reported by different researchers in the literature.[7]

Sr. No.	Study		Source	Incidence %
	Researcher	Year		
1	Pyo	1959	Radiographs	12.60
2	Romanus	1964	Radiographs	14.30
3	Lamberty	1973	Osteologic Specimens	15.00
			Radiographs	7.50
4	Basaloglu	1983	Osteologic Specimens	9.50
5	Stubbs	1991	Radiographs	13.00
6	Cankur	1995	Osteologic Specimens	14.20
7	Mitchell	1998	Osteologic Specimens	9.80
8	Malas	1998	Radiographs	2.60
9	Hassan	2001	Osteologic Specimens	3.40
10	Unur	2004	Radiographs	5.10
11	Present Study	2013	Osteologic Specimens	8.66

Table No.4: Comparison of anteroposterior (AP) and Superoinferior (SI) diameters of the complete arcuate foramen (CAF) in different populations.

Author and population	Complete Arcuate Foramen			
	AP diameter (mm)		SI diameter (mm)	
	Right	Left	Right	Left
Mitchell, 1998, mixed South Africans	6.4	6.6	5.3	5.1
Unur et al, 2004, Turkish	8.2	8.0	5.7	-
Paraskevas et al, 2005, Northern Greek	6.4	6.7	5.4	5.4
Karau et al, 2010, Kenyans	6.29	6.00	5.11	5.16
Present study, 2013, Pakistanis	6.71	6.76	5.07	5.22

A less detailed description is given in radiologic studies, in which arcuate foramen is classified as complete or incomplete.[17] Depending on the method of study, reported incidence changes between 3.4-15% in skeletal bone studies, and between 2.6-14.3% in studies carried out on radiographs (Table-3). In a study involving both the skeletal bones and radiographs of 60 European spines, the reported incidences are 15% and 7.5%, respectively.[7] In general, the radiographic incidence for CAF seems to be lower than that of skeletal bone studies[17], however, variations in different populations and races should also be considered.

In general, the incidence of arcuate foramen is not related with sex. In a study conducted by Unur et al[7] it was concluded that age and sex do not appear to be related to the frequency of occurrence of complete arcuate foramina. Although Stubbs[17] has reported that CAF is more common in males. The age and gender difference of the foramina remained unexplored in our study due to limitations in this regard.

In a study conducted by Mitchell,[10] the incidence of complete retroarticular canal was 9.8%, of which 17% were on the right, 36.1% were on the left and 46.6% were bilateral. The figures in our study 46.15%, 30.77% and 23.08% respectively differ which might be due to ethnic variation.

In our findings for the complete arcuate foramen, the mean anteroposterior (AP) diameter was 6.71 mm on the right and 6.76 mm on the left side. The mean superoinferior (SI) diameter was 5.07 mm on the right and 5.22 mm on the left side. These measurements corroborate with those of the previous workers (Table-4).

Cross- sectional Area of CAF and NFT: There are limited studies comparing the Morphometry of complete arcuate foramen and that of ipsilateral native foramen transversarium. In the present study, the mean area of CAF was found to be 26.74 mm^2 and 27.77mm^2 on the right and left sides respectively. Nearly similar results were obtained by Karau et al[11] which showed mean area of 23.44 mm^2 on the right and 24.98 mm^2 on the left side. But the study of mean area of CAF by Tubbs et al[2] showed 14.2 mm^2 among Iranians and 12.5 mm^2 among Americans. Perhaps this difference might be in part due to ethnic variations and method disparity. The previous workers did not detail the instrument they used, whereas we used the vernier calipers.

The mean cross sectional area of the right native foramina transversaria (NFTs) was 34.86 mm^2 while that of the left was 35.31 mm^2. These findings appear to be similar with those of Karau et al[11] who found 36.30 mm^2 on the right and 37.20 mm^2 on the left NFTs. These readings are higher than that measured among Iranians and Americans by Tubbs et el.[2] It is a notable fact that areas of CAFs are significantly smaller than the area of the ipsilateral NFTs on both sides. The difference in the dimensions of the CAFs and NFTs means that the space for vertebral artery to pass through is reduced, and this may compromise blood flow in the vessel.[11]

Our study supports the previous assertions that presence of complete atlas bridges can lead to compression of the vertebral artery in the absence of arterial disease, and may be an aggravating factor in case of disease.[10,11,16] In extreme manipulations of neck this compression becomes evidently symptomatic.[25] The prevalence of

arcuate foramen in the path of vertebral artery leads to prevalence of compression syndromes. It is possible that the third segment of the vertebral artery may be a reserve length to allow for neck rotation without injury or compression to the artery. Presence of these ponticles may limit this reserve length, predisposing to entrapment of the artery.

Ponticle Thickness: Search of literature revealed that there is paucity of data on the measurement of the ponticle thickness. To our knowledge, only Unur et al[7] measured the mean ponticle thickness on radiographs which was 2.2 mm (1.0-3.5 mm). In our study performed on dried bones, the mean ponticle thickness was 2.64 (1.60 – 3.30 mm) which also needs research in other populations.

CONCLUSION

The prevalence of complete arcuate foramen (CAF) in the atlas vertebrae among Pakistanis are comparable to that in other populations. This study provides information on the morphometry of arcuate foramen and ipsilateral native foramina transversaria (NFTs) and their implications. The observation that CAF are smaller than ipsilateral NFTs suggests that they are an important cause of vertebral artery compression syndromes and needs careful investigations of multifactorial aetiology for the syndromes. Knowledge of CAF may help the surgeons undertaking procedures in the C1 region.

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Original Article

Thalassemia

Serum Ferritin Level in Thalassemic Patients of 10-15 Years and its Relationship with Thyroid Function Tests

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ABSTRACT

Objective: To determine the prevalence of hypothyroidism and to evaluate any possible correlation between serum ferritin level and thyroid function tests in transfusion dependent beta-thalassemic patients.

Study Design: An observational and correlation study.

Place and Duration of Study: This study was conducted at DHQ hospital, Hilal-e-Ahmar hospital and Ali Zaib Foundation hospital Faisalabad from 15th of May 2011 to 15th of Jan 2012.

Materials and Methods: A total number of 90 thalassemia major patients, of 10-15 years of age, were included in this study. Serum levels of thyroxine, tri-iodothyronine, thyroid stimulating hormone were determined and correlated with serum ferritin level. Five milliliters of blood was drawn from each subject and thyroid profile (T_3, T_4 and TSH) and serum ferritin were determined. Pearson correlation coefficient test was applied to determine any correlation between serum ferritin level and other parameters.

Results: There was a weak negative correlation of Serum Ferritin with both Triiodothyronine and Thyroxine, but both correlations were statistically insignificant (p-value= 0.294 & 0.189 respectively). Serum Ferritin had a weak positive, but insignificant correlation with TSH. Hypothyroidism was detected in 15 patients (16.67%). Out of these 8 (8.89%) were having subclinical hypothyroidism, 5 (5.56%) mild hypothyroidism, 1 (1.11%) overt hypothyroidism and 1(1.11%) patient having secondary hypothyroidism.

Conclusion: High prevalence of hypothyroidism warrants regular screening of thyroid functions in thalassemic patients irrespective of their serum ferritin levels.

Key Words: Beta thalassemia, hypothyroidism, Ferritin.

INTRODUCTION

Inherited hemoglobin disorders are the most prevalent single gene defects in human beings across the globe[1], and thalassemia is the commonest in this group[2]. Beta-thalassemia syndromes are a group of hereditary blood disorders characterized by reduced or absent beta (β) globin chain synthesis, resulting in reduced hemoglobin in red blood cells[3]. According to Thalassemia International Federation, about 2,00,000 patients of thalassemia major are alive and receiving treatment globally[3]. In Pakistan, gene frequency of β-thalassemia has been estimated to be 5-8% and about 8-10 million carriers[4] and is present in all ethnic groups[5].

Anemia in these patients is caused by hemolysis and ineffective erythropoiesis, which is characterized by enhanced apoptosis of the maturing nucleated erythroid cells[6,7]. Thalassemia treatment depends on regular blood transfusions but after about one year of transfusions, iron begins to accumulate in parenchymal tissues where it may cause substantial toxicity as compared to that in reticuloendothelial tissues[8].

Because there is no known mechanism to excrete excess iron from the body, repeated transfusions and poor compliance to therapy and chronicity of the disease lead to iron overload- related complications including endocrine dysfunctions[6]. Ferritin is the principal iron storage protein[9], and iron deposits in thalassemics, who have been receiving multiple blood transfusions, can exceed the storage and detoxifying capacity of ferritin, consequently free iron begins to accumulate in the tissues and blood[10].

Thyroid dysfunction in β-thalassemic patients has been reported ranging from a low prevalence of 0-12% to 10-35% in different cohorts[11]. Hypothyroidism is the second major endocrine complication resulting from hemosiderosis[12] Abnormal thyroid functions may be reversible at an early stage through intensive chelation therapy[13].

The aim of the present study was to investigate thyroid hormones and serum ferritin levels and to detect any correlation and presence of hypothyroidism in patients having high serum ferritin level.

MATERIALS AND METHODS

Study Design: The observational and correlation study was conducted on patients recruited from Thalassemia center of District Headquarters Hospital, Ali Zaib Blood Transfusion Services and Thalassemia center of Hilal-e-Ahmar Hospitals, Faisalabad. The study was conducted from 15th of May 2011 to 15th of Jan 2012 (eight months).

Ethical Considerations: Study was conducted as per Helsinki Declaration of Human Rights. Approval was obtained by Ethical Review Committee of Punjab Medical College, Faisalabad. Written informed consent was taken from each patient.

Methodology: Personal data was recorded on a proforma, specifically designed for the study. Patient's age, sex, and blood group etc. were recorded. Five milliliters of venous blood sample was drawn from each child before transfusion. Blood was allowed to clot and serum was separated and stored in freezer, at -80^{o}C, for analysis later on. Following parameters were evaluated.

Serum Thyroid Profile:

1. Triiodothyronine (T_3): For the quantitative determination of the triiodothyronine concentration in the serum, enzyme immunoassay kit was used.
Normal range:- 0.52-1.85 ng/ml

2. Thyroxine (T_4): The total thyroxine concentration was determined using T_4 enzyme immunoassay kit.
Normal range:- Male: 44-108 µg/dl Female: 48-116 µg/dl

3. Serum Thyroid stimulating hormone (TSH): Thyroid stimulating hormone in the serum was determined by Elisa Microwell kit.
Normal range:- 0.39-6.16 µU/ml

4. Serum Ferritin: Serum ferritin levels were determined by using Accu-Bind Elisa Microwell kit.
Normal range:- Male: 16-220 µg/L Female: 10-124 µg/L

Statistical Analysis: The data was analyzed using SPSS version 17.0 (Statistical Package for Social Sciences). Mean ± SEM was calculated for all quantitative variables like (T_3, T_4, TSH and serum ferritin). Pearson correlation coefficient was applied to observed correlation between serum ferritin level and thyroid tests. A p-value of ≤0.05 was considered statistically significant.

RESULTS

In the study there were a total of 90 subjects, out of whom 40(44.44%) were females and 50(55.6%) were males. The male to female ratio is 1.14:1. The mean age of the patients was 12.04 ± 02.0 years.

The most frequently occurring blood group among patients was O^+, constituting 49%; 44 patients out of all 90. The second foremost found blood group was B^+ with 26.7% patients with proceeding group of A^+ comprising 16% of patients. Only 7% patients comprised of all remaining blood groups i.e. A^-, AB^+, B^-, and O^-.

The mean value of Triiodothyronine taken as a whole was 1.146±0.02, with a minimum of 0.30 and a maximum of 1.9. For males the mean value of Triiodothyronine was 1.124±0.04 and for females it was 1.175±0.03. The minimum and maximum values for males were 0.30 and 1.9 and for males 0.8 and 1.5 respectively. There was a significant mean difference of Triiodothyronine observation among males and females (p-value=0.043). Table 1.

Table No.1: Descriptive Statistics of Study Parameters

Parameters\	Mean ± SE		Minimum Value		Maximum Value		p-value
	Male	Female	Male	Female	Male	Female	
Serum Triiodothyronine (ng/ml)	1.124±0.04	1.175± 0.03	0.30	0.80	1.9	1.5	0.043
Serum Thyroxine (µg/dl)	90.24± 41.1	96.59± 32	39	71	142.3	136.5	0.243
Thyroid Stimulating Hormone (µIU/ml)	3.67± 0.69	4.73± 1.20	0.60	0.8	34.6	42.0	0.143
Serum Ferritin (ng/ml)	4601.6±187.5	4996.28±184.60	716.3	2360.0	7616	7070	0.143

For thyroxine, the mean value for all subjects was found to be 93.06±27.0 µg/ml with a minimum of 39.0 and a maximum of 142.30. The average value among males was 90.24±41.1 µg/ml with a minimum of 39.0 and maximum of 142.3. For females, the mean value of thyroxine was 96.59±32.0 µg/ml with a minimum of 71.0 and a maximum of 136.5. There was no significant difference in mean values of thyroxine between both genders (p-value=0.243). (Table-1)

Mean TSH value for all subjects was 4.14±0.65 µU/ml, with a minimum of 0.60 and maximum of 42.00. The minimum value of TSH in males was 0.60 and maximum value was 34.60, whereas among females these values were 0.80 and 42.00 respectively. The mean TSH values were same among both males (3.67±0.69) and females (4.73±1.20) statistically (p-value= 0.424). (Table-1)

The mean±SEM value for serum ferritin for all patients was 4777.04± 133.54 µg/L with a minimum of 716.33 and maximum of 7616.00. The minimum and maximum values among males were 716.33 and 7616.00 µg/L while among females 2360.00 and 7070.00 µg/L respectively. The mean values of serum ferritin were same among males (4601.65± 187.58) and females (4996.28± 184.60) statistically (p-value= 0.143). (Table-1).

According to the severity of ferritin level 85 (94.4%) patients had sever grade while moderate and mild ferritin level was seen in 4(4.4%) and 1(1.1%) patients respectively.

KEY:- Mild = Upto 1000 µg/L Moderate = 1000-2500 µg/L Severe: = More than 2500 µg/L

There was a weak negative correlation of Serum Ferritin with both Triiodothyronine and Thyroxine (Pearson correlation; -0.072 & -0.094 respectively). Both correlation i.e. Serum Ferritin with Triiodothyronine and Thyroxine were statistically insignificant (p-value= 0.294 & 0.189 respectively). **(Figure 1 and 2)**

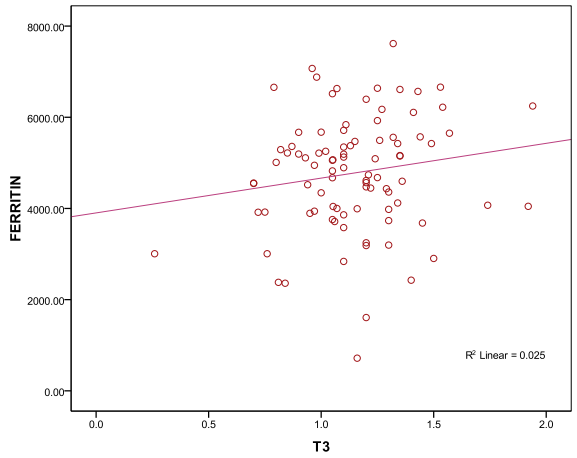

Figure No.1: Scatter plot demonstrating weak negative insignificant correlation in Serum Ferritin and Triiodothyronine

- Pearson correlation = 0.159
- p-value = 0.135 (insignificant correlation)

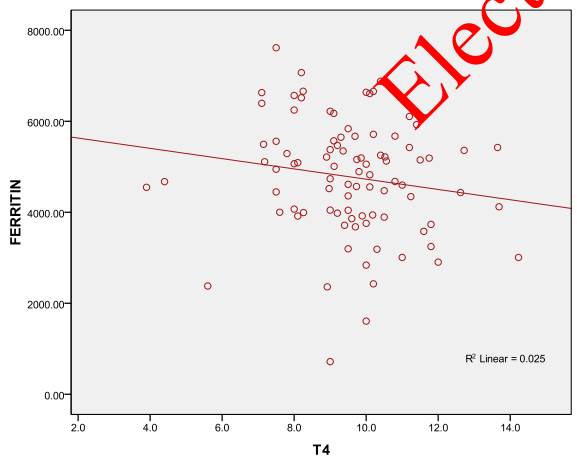

Fig-II: Scatter plot demonstrating weak negative insignificant correlation in Serum Ferritin and Thyroxine

- Pearson correlation = -0.028 p-value = 0.794 (insignificant correlation)
- Serum Ferritin had a weak positive, insignificant correlation with TSH

(Pearson Correlation 0.104; p-value= 0.164), **(Figure 3)**

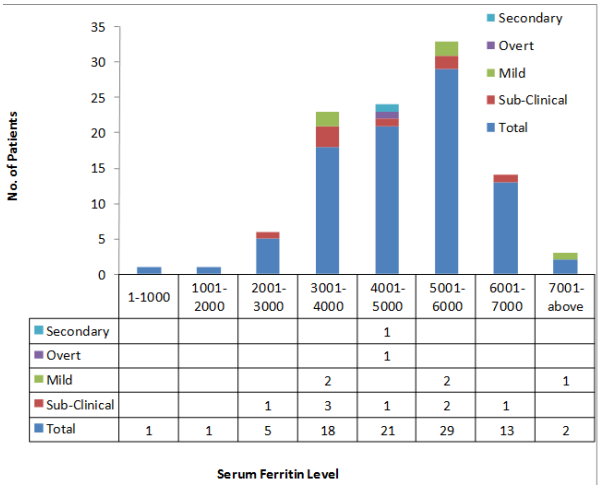

Figure No.4: Comparison of different types of hypothyroidism with serum ferritin level

DISCUSSION

Thalassemia syndromes are the result of a large number of molecular defects that alter the expression of one or more of the globin genes. More than 200 point mutations and rarely deletions have, so far, been described in β-globin gene on chromosome 11, resulting in β-thalassemia[14]. It is common in Mediterranean countries, the Middle East, Central Asia, Indian Subcontinent, Southern China, South East Asia, and Far East [15.16.17].

Programmed repeated blood transfusions, with chelation of iron are the logical therapy for thalassemia patients and have dramatically improved the quality of life and changed it, which was once a fetal disease in early childhood to chronic disease compatible with prolonged life[18]. Now a days life expectancy may extend up to late fifties in some developed countries[15]. These patients have a dramatic increase in iron absorption from the gut which is mediated by down regulation of hepcidin receptors[19.20]. The capacity of serum transferrin, the transport protein to bind and detoxify iron, are exceeded and surplus iron can lead to generation of free radicals from reactive oxygen species via Fenton reaction[21], which can cause tissue damage[22]. ROS include a wide variety of oxygen-, carbon-, and nitrogen- radicals originating from superoxide radicals, hydrogen peroxide and lipid peroxidases[23]. Hydroxy radicals facilitated by membrane associated iron might be particularly harmful because radicals' generation would be relatively sequestered from the cell's antioxidant capacity and occurs directly adjacent to membrane components[24].

Endocrine dysfunction is a frequent complication in thalassemic patients who are on regular transfusions[25]. In some reports, upto 66% patients have at least a single endocrine disorder and 40% have multiple endocrinopathies[26]. Reduced nicotinamide adenine dinucleotide phosphate-induced lipid peroxidation,

cytochrome P-450 inactivation and free radicals production are thought to be the etiology of iron toxicity[27].

Thyroid hormones, thyroxine and triiodothyronine have potent effects on growth, development, and metabolism in almost all tissues of the body, after binding to thyroid hormone receptors [28.29]. Thyroid dysfunction has been reported ranging from a low prevalence of 0-12% to a high prevalence of 10-35% in different cohorts[10]. Hypothyroidism is the second major and well-documented endocrine complication resulting from hemosiderosis[11]. After about one year of transfusions, iron begins to accumulate in parenchymal tissues where it may cause substantial toxicity as compared to that in reticuloendothelial tissues[12].

Results in this study showed that 88 patients (97.8%) had serum ferritin level higher than 2000 µg/L which is very high as compared to levels reported from some developed countries. In these centres only 19 (21.11%) patients got their ferritin levels checked once a year. Hypothyroidism was discovered in 15 patients (16.67%). Out of these 8 patients (8.89%) were having subclinical hypothyroidism with normal serum thyroxine level and slight raised TSH level (≤10 µU/ml). Ferritin level in all these levels was more than 2000 µg/L. Five patients (5.56%) were suffering from mild hypothyroidism with normal T_4 and high TSH levels (more than 10 µU/ml). One patient (1.11%) was diagnosed as having overt hypothyroidism with low T_4 and TSH levels. Ferritin level in this patient was 4548.33 µg/L. Hypothyroidism was not detected in whom serum ferritin level was below 2000 µg/L indicating better control of iron overload and resultantly no thyroid damage.

No significant correlation between ferritin and T_3 and T_4 levels was reported by some other researchers[15.32.].This may be, in part, due to the fact that ferritin levels increase linearly with transfusion overload up to about 100 units of transfused blood, but afterward, there is no simple relationship. Another hypothesis suggested by Pirinccioglu et al is that damage of endocrine glands caused by chronic hypoxia is more prominent than that caused by hemosiderosis.

A high prevalence of hypothyroidism, in patients under study, may be due to ignorance about chelation therapy, its cost and regularity, and carelessness of the parents. Moreover availability of chelating agents and its standardization are some other problems encountered in these centres. Symptoms of hypothyroidism might be confused with that of anemia by clinicians, so at times hypothyroidism might be overlooked especially in adolescent age.

CONCLUSION

In the absence of any significant correlation, it is essential that ferritin level should not be relied upon solely while investigating organ damage in these patients. The role of thyroid hormone in the growth and development in children and availability of hormone replacement therapy necessitates frequent estimation of thyroid status to avert tissue damage and consequent complications.

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Original Article

Pott's Disease

To Determine the Frequency of Pott's Disease in Patient of Parapresis Presenting to Medical Wards of Civil Hospital Karachi

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ABSTRACT

Objective: To determine the frequency of Pott's disease in patients of paraparesis presenting to medical wards of Civil Hospital Karachi.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted in all Medical Wards of Civil Hospital, Karachi, from 1st January 2012 to 31 Dec 2012.

Material and methods: A total of 133 patients of spastic paraparesis & meeting inclusion criteria were included in this study. Inquiry was carried out regarding age, gender, presenting complaints, duration of illness, past history of TB and site of involvement of spine. Diagnosis of Pott's diasease was made on Magnetic Resonance Imaging (MRI) findings of soft tissue edema, disc space narrowing, paraspinal mass or vertebral collapse.

Results: Out of 133 patients, mean age was 47.7 (±15.6) years with male: Female = 1.6: 1. Out of 133 patients of spastic paraparesis, Pott's disease was diagnosed in 53 (39.8%) cases. Frequency of pott's disease was high in male (M: F = 2.1: 1), 36 (43.9%). Average age of patients with pott's disease was 49 ±13.2 years (Min – Max = 22 – 80 years).

Conclusion: In this study Pott's disease was diagnosed in 39.8% patients of spastic paraparesis. Frequency of pott's disease was high in male gender and older (Age: 31 – 50 years) patients.

Key Words: Spinal Tuberculosis, spastic paraparesis, Pott's disease

INTRODUCTION

Tuberculosis (TB) is a major infectious disease of developing countries including Pakistan.[1]

WHO estimated a total of 9.27 million new cases worldwide in 2007 with 13.7 million prevalent cases and 1.3 million deaths with >90% in developing countries. [2] According to WHO estimates in 2009, about 47,587 people died from TB in last five years in Pakistan and about 364,793 cases of TB exists in population.[3]

Five to Ten percent of tuberculosis will have bone and joint infection but the 50% of bone and joint infection is related to spine and called Pott's disease[4]. It is the commonest cause of compression paraplegia. It can cause paraplegia by infecting the vertebrae and compressing the spinal cord.[1\]

Tuberculosis Infection reaches the spine either via the respiratory tract or the intestine by blood stream[5]. The infection begins in the area of the vertebral body. The vertebral body becomes soft and is easily compressed, producing wedging or total collapse[5,6]. The anterior aspect of vertebral body is area usually affected. Tuberculosis may spread from that area to adjacent intervertebral disc. Progressive bone destruction leads to vertebral collapse and kyphosis.[5-8] and leading to paraparesis. India author reported in 2006, Tuberculosis was the commonest cause of compression paraparesis and was observed in 42 cases among 108 patients of paraparesis (33.33%)[9] MRI is the most valuable method for detecting early disease and is preferred technique to define the activity and extent of infection. MR imaging provides clinical information about the spinal cord and the extent of the epidural pus in patients presenting with neurologic deficits. MRI features of tuberculosis infection are soft tissue edema, paraspinal mass, disc space narrowing, vertebral collapse and destruction followed by kyphosis.[10,11]

It is clear from above mentioned data that Tuberculosis and its complications are very prevalent in developing countries including Pakistan. Tuberculous involvement of the spine has the potential to cause serious morbidity, including paraparesis which is regarded as a disease of great and constant misery to the patient, family and the society. So, early diagnosis and treatment is required to treat this reversible cause of paraparesis and prevent fatal outcomes. The aim of this study is to know burden of Pott's disease as a cause of paraparesis in patients coming to large government sector hospital of Karachi and present their key demographics so that early diagnosis and management can be facilitated.

MATERIALS AND METHODS

This study was conducted at Medical department, Civil Hospital Karachi, from 1st January 2012 to 31

Dec 2012. A detailed history of every case was taken and information was noted on a Proforma especially made for study purpose. Inquiry was carried out regarding age, gender and duration of illness. Diagnosis of Pott's diasease was made on Magnetic Resonance Imaging (MRI) findings of vertebral collapse. All patients of spastic paraparesis with no history of trauma, age 18-90 years and duration of illness more than 2 weeks were included in study. Patients presenting to medical wards with non-spastic paraparesis or with history of trauma or duration of illness less than two weeks were excluded.

RESULTS

A total of 133 patients with spastic paraparesis with duration of illness more than 2 weeks were included in this study. Gender distribution showed male preponderance (male: female = 1.6: 1) There were 82 (61.7%) males and 51 (38.3%) females (Table 1). Mean (±SD) age of patients was 47.7 (±15.6) years with min – max = 18 – 90 years. Majority of cases were in the age groups 31 – 70 years, 98 (73.7%) (Table 2).

Tale No.1: Pott's disease with respect to gender n = 133

Gender	Total	Pott's disease	Percentage
Male	82	36	43.9%
Female	51	17	33.3%

Table No.2: Variables of Pott's Disease n = 133

Variable	**Patients**	**Percentage**
Age in years (Mean ±SD = 47.7 ±15.6 years)		
≤ 30	28	21.1
31 - 50	49	36.8
51 - 70	49	36.8
71 - 90	7	5.3
Duration of Illness (Mean ±SD = 9.9 ±9.5 months)		
≥ 1	44	33.1%
< 1	89	66.9%
Pott's Disease in Cases With Paraparesis		
Present	53	39.8%
Absent	80	60.2%

Duration of illness (spastic paraparesis) was 9.9 ±9.5 months with min – max was 1 month – 5 years. In majority 89 (66.9%) of cases duration of cirrhosis was < 1 year (Table 1). Out of 133 patients of spastic paraparesis, Pott's disease was diagnosed in 53 (39.8%) cases . Frequency of pott's disease was high in male, 36 (43.9%),(M: F = 2.1: 1) (Table 1). Average age of patients with pott's disease was 49 ±13.2 years (Min – Max = 22 – 80 years). Frequency of pott's disese was high in age 31 - 50 years, 27 (55.1%). Table-1 Duration of spastic paraparesis and pott's disease is shown in Table-4. Mean duration of cases with pott's disease was 9.2 ±7 months (Min – Max = 1 month – 3 years).

DISCUSSION

Paraplegia is conditions with considerable morbidity having tremendous social repercussions. It is regarded as a disease of great and constant misery to the patient, family and the society. It is estimated that involvement of the spine occurs in less than 1% of patients with tuberculosis[9] and accounts for 40-50% of musculoskeletal tuberculosis[12,13]. It results from an infection of the bone by Mycobacterium tuberculosis bacteria through a combination of haematogenous route and lymphatic drainage. The organism may stay dormant in the skeletal system for an extended period of time before the disease can be detected. The basic lesion may be a combination of osteomyelitis and arthritis. Spinal cord may become involved in compression by bony elements and/or expanding abscess or by direct involvement of cord and leptomeninges by granulation tissue. Neurological deficit are usually more symmetrical and of more gradual onset than those resulting from other pathologies[14]. Typically, more than one vertebra is involved and more than one component of the spine is involved namely the vertebral body, intervertebral disc and the ligaments, paravertebral soft tissues and the epidural space[15]. The condition most commonly involve the lower thoracic and the thoraco-lumbar spine[16].

MRI is the most valuable method for detecting early disease and is preferred technique to define the activity and extent of infection. MR imaging provides clinical information about the spinal cord and the extent of the epidural pus in patients presenting with neurologic deficits. MRI features of tuberculosis infection are soft tissue edema, paraspinal mass, disc space narrowing, vertebral collapse and destruction followed by kyphosis.[10,11]

In this study 133 patients with spastic paraparesis were included in this study. Gender distribution showed male preponderance (male: female = 1.6: 1). Mean (±SD) age of patients was 47.7 (±15.6). The male preponderance of 72% possibly portrays differential gender hospital attendance pattern in the region of the study as women often dependant to go to the hospital. A similar pattern has been reported in some other developing countries[17,18].

Out of 133 patients of spastic paraparesis, Pott's disease was diagnosed in 53 (39.8%) cases. In a study done in India in 2006, Tuberculosis was the commonest cause of compression paraparesis and was observed in 42 cases among 108 patients of paraparesis (33.33%).[9] In two separate studies reported in Africa in 1994 and 1995 tuberculosis was the leading cause of paraplegia accounting for 29.69% cases and 47% cases[19,20]. In a study done in Nigeria in 2011,

Tuberculosis was the commonest cause of compression paraparesis and was observed in 44 cases among 98 patients of paraparesis (44.9%)[17]. In studies reported in the other parts of Africa as well as developing countries outside the African continent, tuberculosis was the leading cause of paraplegia accounting for between 29.69 and 47% cases[20,21,22]. However, in a Zimbabwean study, neoplasm was reported to be the commonest (28%) cause of non-traumatic paraplegia, followed by tuberculosis (27%)[22].

Frequency of pott's disease was high in male (M: F = 2.1: 1), 36 (43.9%). Average age of patients with pott's disease was 49 ±13.2 years (Min – Max = 22 – 80 years). Frequency of pott's disese was high in age 31 - 50 years, 27 (55.1%). Mean duration of cases with pott's disease was 9.2 ±7 months (Min – Max = 1 month – 3 years).

It is clear from above mentioned data that Tuberculosis and its complications are very prevalent in developing countries including Pakistan. Tuberculous involvement of the spine has the potential to cause serious morbidity, including paraparesis which is regarded as a disease of great and constant misery to the patient, family and the society. So, early diagnosis and treatment is required to treat this reversible cause of paraparesis and prevent fatal outcomes.

CONCLUSION

In this study Pott's disease was diagnosed in 39.8% patients of spastic paraparesis. Frequency of pott's disease was high in male gender and older (Age: 31 – 50 years) patients. On the basis of results of this study tuberculous involvement of the spine has the potential to cause serious morbidity, including paraparesis which is regarded as a disease of great and constant misery to the patient, family and the society.

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Original Article

Teratogenic Effects of Different Concentrations of Retinoic Acid on Chick Embryonic Heart Cells Cultured in Vitro

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ABSTRACT

Objective: To detect the possible teratogenic effects of various concentrations of retinoic acid (RA), in chick cardiac cells cultured in micromass culture.

Study Design: Experimental study

Place and Duration of Study: This study was carried out at the University of Nottingham, UK on chick embryonic hearts for a period of six months from Jan. 2010 to June 2010.

Materials and Methods: Embryonic hearts were dissected from 5 day old white leghorn chick embryos to produce a cardiac cell suspension in DMEM culture medium. Cells were either exposed to culture medium or vehicle only or to different concentrations of retinoic acid ranging from1 µM to 100 µM. End points for cellular differentiation were observational scores at 24, 48 and 144 h following explantation. Cell viability was established with resazurin and kenacid blue assays. Statistical analysis of the results was via one way ANOVA and Kruskal Wallis tests and *P*-value < 0.05 was considered significant.

Results: Retinoic acid significantly reduced cellular differentiation at and above 1 µM (*P* value < 0.05), at concentrations 50 µM and above no single focus was observed to be beating. The resazurin assay for viability showed decreasing viability of cardiac cells with increasing concentrations of retinoic acid. Same trend was observed with kenacid blue assay which determined the overall protein content. However the cells exposed to only culture medium or vehicle did not show significant differences in terms of viability, protein content and beating ability.

Conclusion: The potential of retinoic acid as teratogen is proved in this in vitro study and it is recommended that the pregnant ladies should avoid the use of these drugs during early developmental period.

Key Words: Chick Embryonic Hearts, Micromass Culture, Retinoic Acid

INTRODUCTION

Retinoic acid plays an essential role in cell proliferation, differentiation, vision, reproduction and immune functions[1]. Apart from these functions, retinoic acid is used as prevention of acute promyelocytic leukemia [2]. Isotretinoin, a retinoic acid compound, is effective in treating dermatologic disorders, including the treatment of severe, reluctant nodular acne which is refractory to conventional therapy[3].

Retinoic acid also plays an important role during embryonic life, where it influences development of several organs including hind brain, heart, spinal cord, kidneys, and limb buds [4].

Although these compounds are important for adult and embryonic life but, their excess and deficiency results in abnormal homeostasis including birth defects. A combination of birth defects known as retinoic acid embryopathy are produced by excessive intake of retinoids [5] , while its deficiency or absence causes embryonic segmentation, growth failure and eventual resorption. These considerations make it necessary to maintain retinoid homeostasis during developmental processes. The main sources of the preformed vitamin include animal foods (dairy products, liver, eggs etc.), fortified foods and pharmaceutical supplements, while several fruits and green leafy vegetables constitute rich sources for the provitamin form or carotenoids [6]. The major organs affected during developmental process by excessive amounts of retinoids include heart, brain and craniofacial areas. Adverse effects on heart include either lack or fusion of the paired cardiac primordia, impaired or reversed heart looping and truncation of the posterior portion of the heart tube with abnormal expansion of anterior structures. Retinoids exert their pleiotropic effects through binding to two families of nuclear receptors, named as retinoic acid receptors (RARs) and retinoic X receptors (RXRs) [7]. This study is carried out to evaluate the effects of different doses of retinoic acid on micromass culture of chick embryonic hearts.

MATERIALS AND METHODS

This experimental study was carried out at the University of Nottingham, UK on chick embryonic hearts over a period of six months.

Fertile white leghorn chicken eggs were labelled with the date of delivery and stored in a cooled incubator at 12-14^{o}C until required and used within two weeks of being laid. The eggs were placed onto the automated egg turner and incubated at 38^{o}C with relative humidity of 100% for 5 days, day zero being defined as the day when the eggs were set in the incubator. A minimum of 24 eggs were incubated for each micromass system to ensure the availability of enough viable embryos. All the embryos were killed by decapitation after being removed from incubator.

Micromass culture:

Eggs were removed from the incubator, six at a time and transferred to the culture hood. Using the blunt end of the curved forceps the broader end of the eggs (near air sac region) was struck until the broken shell could be gently removed and discarded. The shell and all the membranes including vitelline membranes were removed with the help of sterile forceps to expose the embryo. The embryo was lifted from the egg with curved forceps and placed into a petri dish containing Hanks balanced salt solution (HBSS).

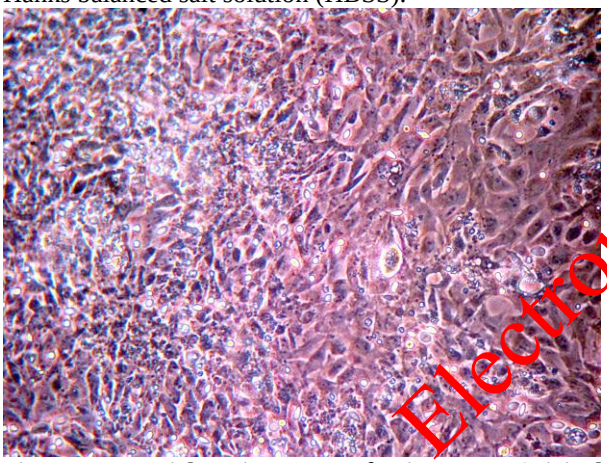

Figure No.1: Light microscopy of micromass. Original magnification x200 (Pic. By Helena Hurst).

After removing the allantois and remaining amnion, under the dissecting microscope the heart was taken out from the embryo and transferred using sterile forceps to a sterile universal tube containing horse serum (50% v/v in HBSS) and stored on ice. Once all the hearts had been collected, the solution of horse serum (50% v/v in HBSS) was removed and tissues were washed twice with HBSS. Heart tissue was incubated in 4ml of trypsin/ETDA (for 24 eggs) at 37^{o}C in 5 %(v/v) CO_2 in air for 20 minutes, agitating every 5 minutes for further disassociation of tissue. The solution was triturated numerous times in order to break the tissues as much as possible. To inhibit further actions of trypsin 6ml of DMEM culture medium was added. Samples were centrifuged at 1500rpm for 5 minutes, the supernatant was removed and the pellet resuspended in 1ml of warmed DMEM culture medium. Cell density was established using a haemocytometer and the cell suspension diluted to 3x10^{6} cells/ml. A 20µl aliquot of the cell suspension was pipetted on to the centre of the well within a 24 well plate for about two and half hours, to allow them to attach, before being flooded with 500µl of prewarmed culture medium(DMEM) and returned to the incubator for 24 hours to recover.

Scoring method for cardiomyocyte activity: A numerical morphological scoring system was constructed to determine the amount of contractile activity observed for heart micromass (MM) as shown in table 1.

Table No.1: Morphological scoring system to determine contractile activity of cardiomyocytes

Numerical morphological score	Contractile activity
0	No contractile activity
1	Few contracting foci
2	Numerous contracting foci
3	Entire plate contracting
Morphological score	**Pace of contractile activity**
S	Low
M	Medium
F	Fast

Retinoic acid preparation: All-trans retinoic acid (Sigma-Aldrich) is a fat soluble vitamin, so, after weighing out the desired amount in a fume cupboard, the yellow coloured retinoic acid powder was dissolved in 100% ethanol to prepare the stock solution and serially diluted in DMEM culture medium to obtain the test concentrations, ranging between 1 and 100µM. Chemicals were made up at twice the concentration required as 500µl of test solution was added to the 500µl culture medium already present in the 24 well plate, which gave the required concentration. All the test chemicals were made up the day to be used and applied to the MM cultures 24 hours after they were seeded.

Resazurin conversion assay: The resazurin assay was performed on day 6 following explantation. The resazurin stock (100µg/ml) solution was diluted 1:10 in sterile HBSS and warmed to 37^{o}C in water bath prior to use. The medium was removed from the 24 well plates and replaced with 500µl resazurin solution. The plates were then incubated for one hour at 37^{o}C and 5% (v/v) CO_2 in air. The optical density was read using a FLUOR star plate reader, excitation wavelength of -530±12.5nm, with a gain of 10. The data was expressed as the increase in optical density above the non-cell blank as a percentage of the untreated cultures. Analyses of data, for statistically significant differences, were performed on the raw data. If repeat assays were performed, once the plate had been read in the spectrofluorimeter, the resazurin solution was

removed and the cells were fixed with 300µl of kenacid blue fixative. The plates were then kept in refrigerator until the kenacid blue assay was performed.

Kenacid blue total protein assay: Wells were aspirated and 300µl kenacid blue fixative was added and allowed to evaporate overnight at 4°C. Kenacid blue working solution (400µl) (Knox et al, 1986) was added to each well and the plate placed on a plate shaker for at least 2 hours. Excess stain was removed and cells were quickly rinsed in 400µl of washing solution before being washed for 20 minutes with agitation. The washing solution was replaced with 400µl of desorb and gently agitated on the plate shaker for one hour. The optical density was read on an ASYS HITEC Expert 96 plate reader with a reference filter of 405nm, and a reading filter of 570nm. The amount of protein per well was calculated from standard curves.

Statistical analyses: The data was calculated in Prism 5 software and analysed using an ANOVA (one way) assay with the post hoc Dunnets test for parametric data. For nonparametric data (scoring of cells), a Kruskal-Wallis test was performed and a Dunn's post hoc test was used to test the significance. In all cases p value < 0.05 was considered significant.

RESULTS

The aim of this study was to detect with a range of retinoic acid concentrations the potential to produce teratogenic effects on cardiomyocytes in micromass culture. Concentrations of altrans retinoic acid tested ranged between 1µM to 100µM. Results for resorufin production, a test for cell viability are shown in fig 3.

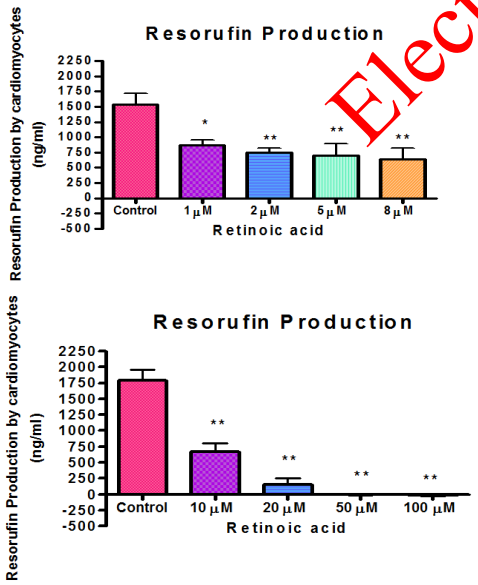

Figure No.2: Showing resorufin content of cardiomyocytes, treated with various concentrations of all-trans retinoic acid

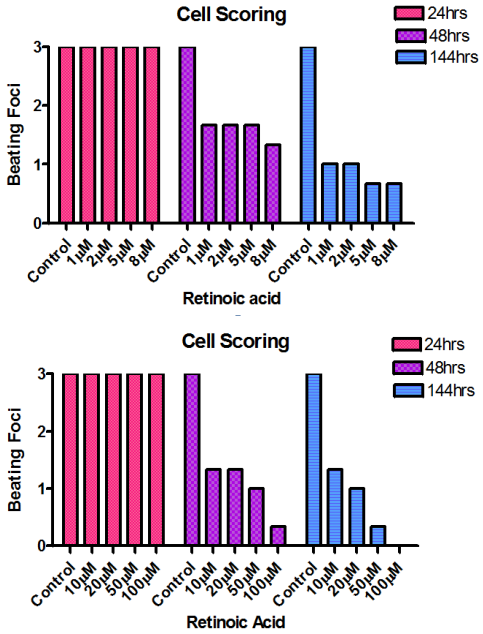

Figure No.3: Showing cell scoring of cardiomyocytes, treated with various concentrations of all-trans retinoic acid.

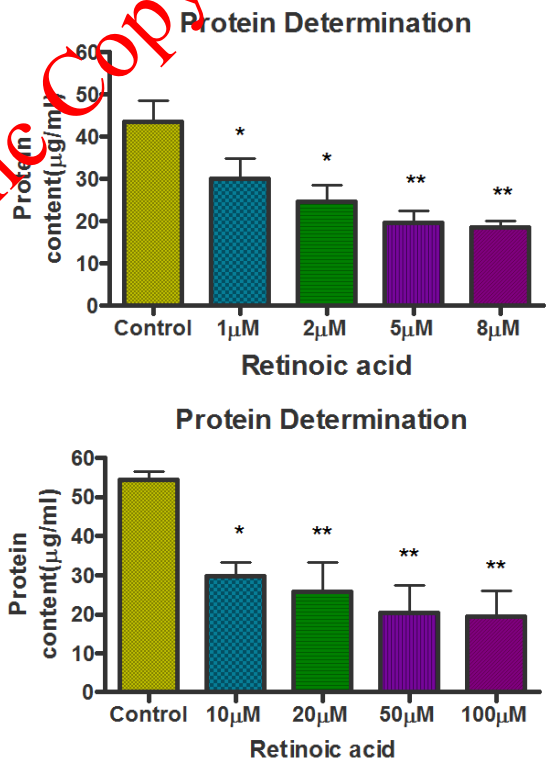

Figure No.4: Showing Protein content of cardiomyocytes treated with various concentrations of all-trans retinoic acid.

DISCUSSION

Retinoids are known human teratogens and therefore have been extensively investigated. This study was aimed to prevent the teratogenic effects retinoic acid by supplementary folic acid.

The teratogenic potential of altrans retinoic acid on chick micromass culture was confirmed by our present work. The effects were consistent for any of the three end points measured. The reliability of chick MM culture was tested by [8], with retinoic acid one of the test chemicals used to treat the limb buds. Results reflected those found in our study, with inhibition of cellular differentiation, cell viability and protein synthesis in chick cardiomyocytes MM cultures exposed to all-trans retinoic acid.

Many animal studies have focused the teratogenic effects of retinoids on developing heart cells. In an investigation on effects of retinoic acid on early heart development by [5],[9] he found that the retinoic acid produced a wide range of heart malformation when applied either to the whole embryo culture or implanting in the form of beads to the precardiac mesoderm same were observed in other species. In both of these experiments the embryos were treated with concentrations of retinoic acid ranging from 1µM to 100µM. Although supporting the current study in some ways, Osmond et al did not find any killing of cells even at higher concentrations of retinoic acid. In contrast our study showed cell death at concentrations ranging from 20µM to 100µM.

In another study conducted on mouse whole embryo culture Zhang et al 2006, found large number of malformation including cranial NTDs,and branchial arch abnormalities were found in 100% of embryos exposed to 0.4µM concentration of retinoic acid. The reason of cell death in our study on micromass system could be due to high concentrations of retinoic acid used or increased sensitivity of the micromass to retinoic acid, because in micromass culture the cells are in direct contact with the retinoic acid whereas in whole embryo culture the embryo is protected by the surrounding membranes and yolk sac.

It is not possible to relate our findings of teratogenic levels of retinoic acid with humans; however, it is apparent from case studies that the human embryos are being exposed to damaging levels of retinoic acid. An epidemiologic study conducted by (1) on women who took an average of >10000 IU of retinol/day in the form of supplements revealed that they had a higher proportion of babies born with birth defects. Another recent study (Barbero et al, 2004) describes a child suffering from congenital anomalies due to retinoic acid embryopathy following treatment of the mother's acne with 10mg/day of acitretin, a retinoid, despite treatment being stopped over a year pre-conception.

CONCLUSION

The potential of retinoic acid as teratogen at higher concentrations when given at early embryonic age is proved in this in vitro cell culture study.

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Original Article

Lap. VS Open Appendectomy

To Compare the Frequency of Superficial Surgical Site Infection After Laparoscopic Versus Open Appendectomy

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ABSTRACT

Objective: To compare the frequency of Superficial Surgical Site infection after laparoscopic versus open appendectomy.

Study Design: Randomized clinical trial study

Place and Duration of Study: This study was conducted at Surgical Department Jinnah Post Graduate Medical Centre Karachi and Dow University Hospital from August 2013 to January 2014.

Materials and Methods: The source of data was patients admitted in emergency. Patients were selected on the basis of clinical features. The data was collected with the help of Performa attached. It included demographic data of the patient, presenting complaints, operative findings, Surgical site infection. Random patients were placed in two groups. Surgical site infection by observation of pain, redness, tenderness and purulent discharge from the wound. Patients included were of both gender and age above 13 years presented to emergency department diagnosed as acute appendicitis on the basis of history and examination and exclusion of under 12 years of age, appendicular mass, CLD, I.H.D , DM and renal failure.

Results: Out of 270 patients, 153(56.7%) patients were males and 117(43.3%) patients were female. In Present study the different operative findings with their distribution among gender are shown in table. In other findings three patients with ruptured ovarian cyst and one with Mackel's Diverticulitis in which procedure was converted to open and resection and anastomosis of small intestine was done. SSSI is found to associated with operative finding with a significant P value 0.001.

Superficial Surgical Site Infection were observed in both procedure laparoscopic appendectomy allotted in 134 cases but four cases are converted to open procedure so they are excluded from the results. The reason for conversion in three cases was difficulty in mobilizing the appendix because of adhesion and in one case Mackel's Diverticulitis found which need open procedure for formal small intestine resection and anastomosis. Superficial Surgical Site Infection was observed in three cases of Laparoscopic appendectomy and in 15 cases of Open Appendectomy group with the P value 0.005.

Conclusion: Laparoscopic appendectomy is a better choice because of its reduced frequency of SSSI when compared with open procedure. SSSI is an important complication.

Key Words: Appendicitis, Laparoscopic Appendectomy, Open Appendectomy, SSSI

INTRODUCTION

Appendicitis is a most common surgical emergency, with a life time risk of 6%[1]. Diagnosis of appendicitis is very important in making the decision as there are other conditions presented with symptom alike appendicitis. Diagnosis depend on the clinical picture, Investigations and aided by imaging like Ultrasonography and CT Scan. Different scoring systems was advised to help in the decision making like Alvarado scoring system which was later on changed as Modified Alvarado Scoring. Laparoscopic appendectomy done first time by a German gynecologist Semm in 19811.After that a debate started regarding which procedure is better with a less rate of complication. Many studies have been conducted to compare the two procedure regarding operative time, postoperative wound infection, early mobilization, intra abdominal abscess, postoperative fever, and hospital stay[2]. Laparoscopic appendectomy was found superior than open appendectomy in most of the studies regarding the wound infection which is significantly reduced after laparoscopic appendectomy and statistically non significant increase in number of intra abdominal abscess formation after laparoscopic appendectomy [1,2] but according to other study there is no statistical difference between the out come of two procedure regarding the wound infection(6.2% versus 6.7%) but the intra abdominal abscess rate(5.3% versus 3%) and operative time(80 min. versus 60 min). is more after the laparoscopic than after open appendectomy [3].

Surgical site infection is one most common complication after open appendectomy. It has been observed by studies that wound infection is reduced (from 4-6 percent in open appendectomy to 0.4-0.6 percent) in laparoscopic appendectomy[2,4,5,6] It is because of this reason that in most centers of the world where facilities and expertise of Minimal Access Surgery are available, Laparoscopic appendectomy has become the standard procedure for this pathology. We have developed a new technique of manipulating appendix in laparoscopic appendectomy. This includes holding of appendix with endograsper while dissecting, coagulating mesoappendix and placing loop knot. Similarly with this technique the appendix is delivered through 10mm port without touching the skin wound. This study aims at evaluation of laparoscopic appendectomy and its comparison with open surgical technique. The outcome of this study would be a guide line and documented local reference for the surgeons who are working in the field

MATERIALS AND METHODS

This is randomized clinical trial study conducted at at Surgical Department Jinnah Post Graduate Medical Centre Karachi and Dow University Hospital from August 2013 to January 2014.

The patients were selected on the basis of clinical features. All patients were operated after informed consent by the senior registrar and consultant surgeon. Data were include demographic data of the patient, presenting complaints, operative findings, SSSI. Random patients are placed in two groups. Surgical site infection observation is pain, redness, tenderness and purulent discharge from the wound. Discharge criteria is when bowel sound audible and patient taking orally. Stitches are removed on 7th postoperative day. Follow up visits on day 3rd, 7th and 15th. Follow up were ensured by taking telephonic contact of patients. The findings were recorded by trainee researcher.

RESULTS

The results of the analysis of data on 270 patients underwent Appendectomy according to their allocated protocol. Patients were categorized into 2 groups; A: open appendectomy B: laparoscopic appendectomy. Our study population was in age group of 13 to 60 years. Mean age of patients in Laparoscopic group is 23.21 yrs, whereas it is 25.10yrs in Open group. (Table 1).

Out of 270 patients, 153(56.7%) patients were males and 117(43.3%) patients were female. In Present study the different operative findings with their distribution among gender are shown in table. In other findings three patients with ruptured ovarian cyst and one with Mackel's Diverticulitis in which procedure was converted to open and resection and anastomosis of small intestine was done. SSSI is found to associated with operative finding with a significant P value 0.001.

Superficial Surgical Site Infection were observed in both procedure laparoscopic appendectomy allotted in 134 cases but four cases are converted to open procedure so they are excluded from the results. The reason for conversion in three cases was difficulty in mobilizing the appendix because of adhesion and in one case Mackel's Diverticulitis found which need open procedure for formal small intestine resection and anastomosis. Superficial Surgical Site Infection was observed in three cases of Laparoscopic appendectomy and in 15 cases of Open Appendectomy group with the P value 0.005.

Table No.1: Showing Age in both groups

Procedure Performed	Mean age	N	Std. Deviation
Laparosopic	23.21	134	7.511
Open	25.10	136	8.654

Table No.2: Relation of SSSI with operative finding

Peropative Finding	SSSI			Chi-Square Test
	No	Yes	Total	
Acutely inflamed	213	13	226	0.024
Perforated	12	4	16	
Normal	23	1	24	
Others	4	0	4	

Table No.3: Incidence of SSSI among groups

Procedure performed	SSSI			Chi-Square Test
	No	Yes	Percentage	
Laparoscopic Appendectomy	3	127	2.30%	0.005
Open Appendectomy	15	121	11.02%	
Total	18	248	6.76%	

DISCUSSION

Appendectomy can be performed by open or laparoscopic. These are the two different techniques. Open appendectomy is done though different surgical incisions like McBurney's ,Lanz and Rutherford depending on the clinical assessment and the stage of inflammation of appendix. In Laparoscopic appendectomy different techniques are introduced like 3 port, 2 port and even with single port.

Superficial Surgical Site Infection is an important complication following any surgical procedure because it increase the morbidity of patients and increases the burden on the health resources. By reducing the SSSI we can improve the outcome of procedure and early recovery of patients.Despite the surgical procedure

there are different other factors responsible for the development of SSSI.

In our study showed the frequency of SSSI in Laparoscopic appendectomy is 3 out of 130 procedures. And 15 patients develop SSSI in open group out of 136. P value is 0.005 which is less than 0.05 means it is statistically significant value. The Probable reason of decreased in SSSI in Laparoscopic appendectomy are that the inflamed appendix did not make a direct contact with the skin incision which may be the case in open appendectomy. And the minimum tissue dissection at the incision site. I have followed the patients for 15 days postoperatively. There is a possibility of missing some of the cases of Superficial Surgical Site Infection because as per definition of Superficial Surgical Site Infection can occurs within 30 days of operation.

Result of my study is compatible with the Cochrane review which was published in 2010 which includes about 56 studies comparing the Laparoscopic versus open appendectomy and concluded that the wound infection is less after laparoscopic appendectomy (3.8% as compared to 7.6%) The other parameters were also compared like post operative pain, hospital stay and return to normal activity showed improve result in laparoscopic appendectomy. But some of the parameters like operative time, intra-abdominal abscesses formation and cost of procedure are not in favors of laparoscopic appendectomy[7].

Another study conducted at St. Joseph's Hospital in Edmonton. The study subject are 175 adult patients who were operated Laparoscopically with the diagnosis of appendicitis from 1995 to 2002. The infectious complications observed post operatively in which 1 is wound infection and other is intra-abdominal collection and the percentage of wound infection in this study was 0.57[8].

A study conducted over a period of 1 year in India also prove the lower incidence of wound infection after Laparoscopic appendectomy. In this study 100 patients with Laparoscopic appendectomy compared with 179 patients with open appendectomy. Wound infection develop in 4% of Laparoscopic group and 14% in open group[9].

Studies done in our country are also in favor of laparoscopic appendectomy in term of decrease in wound infection. A study conducted at Liaquat University of Medical and Health Sciences Jamshoro. A total of 100 patients studied in which 48 underwent laparosopic appendectomy and 52 were of open appendectomy. 3 patients in laparoscopic group develop wound infection as compared to 7 patients in open group but the P value is statistically not significant [10].

A study conducted at Lady Reading Hospital Peshawar. In which each group consisted of 60 patients. The parameters are Operative time, postoperative pain, intra and post operative complications including wound infection, hospital stay and return to normal daily activity. Wound infection was 8.3% in open group and 1.6% in laparoscopic group with the P value 0.005. other parameters also in favor of laparoscopic appendectomy[11].

The other aspect of cosmetic improvement in appendectomy is by decreasing the size of abdominal port and using the natural orifice like vagina but limited work has been done in these lines [12,13].

CONCLUSION

Laparoscopic Procedure is a better choice in case of appendectomy because of its reduced frequency of SSSI when compared with open procedure. SSSI is an important complication leading to delay in recovery of patient and increases burden on the economics of health. Laparoscopic Appendectomy should be a preferred approach where facilities and expertise are available.

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Original Article

HIV AIDS

Response of Antiretroviral Therapy (Ziduvidune, Lamivudine, Niverapine) in Patients Suffering from Acquired Immuno Deficiency Syndrome (AIDS)

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ABSTRACT

Objective: Purpose of current study was to evaluate the effect of antiretroviral drugs (Three regimen) Ziduvodine, Lamivudine and Niverapine to HIV patients presented in D.G. Khan Zone in regard to CD4 level and viral loads before start of drugs and after one year treatment.

Study Design: Comparative study

Place and Duration of Study: This study was carried out at the Institute of Molecular Biology and Biotechnology, and Centre for Research in Molecular Medicine, The University of Lahore-Pakistan from April 2013 to June 2014.

Materials and methods: Seventy five (75) patients suffering from HIV and thirteen (13) control individuals were selected for the study. Rapid testing and ELISA screening were performed for identification of presence/absence of virus and antibodies respectively. Viral load and CD4+ absolute count were also evaluated by PCR and Multiset software respectively. All the analytical work was performed at the Institute of molecular biology and biotechnology (IMBB), and Centre for research in molecular medicine (CRiMM), The University of Lahore-Pakistan.

Results: Statistically highly significant difference (P=.000) was observed regarding viral load before and after the treatment in HIV patients receiving combination therapy ART (antiretroviral therapy). The viral load in control and HIV patients before and after the treatment was (0.00, $3.23x10^4$) and (0.00, $1.45x10^2$) respectively. Levels of CD4+ cells were increased and a highly significant difference was recorded among control and ART treated patients. Inverse correlation was recorded between viral loads (After) and CD4+ levels (After), (Viral Load Vs CD4+, r = -.678**).

Conclusion: It can be concluded that ART is highly effective in AIDS patients with minimal adverse effects, makes the life of AIDS patients less miserable and improve the quality of life.

Key Words: Antiretroviral drugs, ART, Ziduvodine, Lamivudine, Niverapine, ELISA, CD4+, PCR, viral load, HIV AIDS.

INTRODUCTION

Human Immuno deficiency virus was discovered in 1983. Initially it was mainly found in the people who were involved in homo sexuality also named as Gay cancer. It is believed that this virus is transmitted from animals to human beings. It is believed that it is a virus generated in labs to be used in biological weapons but eventually escaped and later entered in the genome of animals from where it is transmitted to human beings (WHO, 2009)[1]. On the clinical manifestations, the disease was named as Acquired immunodeficiency Syndrome with acronym of AIDS. ART is recommended for all people infected with HIV. ART involves taking a combination of anti-HIV medication (a regimen). Everyday ART is a lifelong treatment (Zhou et al., 2010)[2]. The detection of a virus from the lymphocytes of the AIDS patients was done in 1984 independently by Robert Gallo at the National Institute of Health, USA and Montagnier at the Pasteur Institute, Pairs.

According to the WHO committee on AIDS in (2009)[1] stated, that prevention of HIV infection should be the most seeking task as disease was spreading very rapidly. A joint venture for awareness, pre-cautions, prevention & treatment should be initiated and managed accordingly with different stake holders like Government Institutions NGOs, Pharmaceutical Industry and research institution. Nucleoside reverse transcriptase inhibitors (NRTIs), Non nucleoside reverse transcriptase inhibitors, (NNRTIs), protein inhibitors and some other drugs are also available that inhibit viral process to make copies of itself.

MATERIALS AND METHODS

Inclusion criteria for studies: Patients form both genders, ages groups include children up to 60 years of age. The study was conducted from April 2013 to June

2014. Seventy five (75) patients suffering from HIV and thirteen (13) control individuals were selected for the study from Dera Ghazi Khan. All the analytical work was performed at the Institute of molecular biology and biotechnology (IMBB), and Centre for research in molecular medicine (CRiMM), The University of Lahore-Pakistan.

Following criteria was adopted to start anti-retro viral therapy.

1. Patient was a confirmed case of HIV/AIDS by rapid testing, by ELISA screening of detection of anti bodies and viral load by PCR.
2. CD4 absolute count. CD4 absolute count should be less than 350 cells/micro ml (normal range 450-1100)
3. Clinical Staging of the patients was determined.
4. Incidence of repeated opportunistic infection along with repeated Diarrhea.

Exclusion criteria:

1. Age above 70 years
2. CD4 absolute count more than 350 cells/micro ml.
3. Patient not willing to start antiretroviral therapy.

Methodology:

Rapid testing: 3CC of venous blood was taken and centrifuged, serum was separated and put on rapid kit along with buffer if 2 lines are appearing patient was positive. In case of negative only control line appeared on device. The first line was for control and second line was for patient (test).

ELISA Screening: Antibodies were detected by sandwich method of labeled prefilled antigen-antibody mixture and were compared with cut off ratio and determined the reactivity.

Viral Load by PCR: PCR facility was provided by Centre for Research in Molecular Medicine (CRiMM) and Institute of Molecular Biology and Biotechnology (IMBB), the University of Lahore, Lahore.

CD4 absolute Count: The absolute CD4 & CD8 count (absolute number of positive cellular events in sample compared to beads events) was determined by Multiset software and expressed in cells/ µl.

RESULTS

Data presented in Table-1 shows statistically highly significant difference (P=.000) was observed regarding viral load before and after the treatment in HIV patients receiving combination therapy, ART (Ziduvidune-Lamivudine-Niverapine). The viral load in control and HIV patients before and after the treatment was (0.00, $3.23x10^4$) and (0.00, $1.45x10^2$) respectively. The data regarding CD4+ cells depicted in table 01 also shows that with combination therapy, ART (Ziduvidune-Lamivudine-Niverapine), the levels of CD4+ cells was increased and a highly significant difference was recorded among control and ART treated patients. The CD4+ cells levels in control and HIV patients before and after the treatment was (340.38, 196.77) and (188.59, 388.33) respectively. Data in table 03 (Pearson Correlation, Two Tailed**)** shows that a highly significant inverse relationship between viral load (Before) and CD4+ cell levels (Before) (Viral Load Vs CD4+, r = -.633**). Likewise inverse correlation was also recorded between viral loads (After) and CD4+ levels (After), (Viral Load Vs CD4+, r = -.678**).

Table No.1: Comparison of viral load and CD4+ among control and patients

	Group	n	Mean±SD	P value
Viral load (before)	Control	13	0.00±0.00	.000
	Patient	75	$3.23x10^4$±0.67	
Viral load (after)	Control	13	0.00±0.00	.000
	Patient	75	$1.45x10^2$±0.24	
CD4+ (before)	Control	13	340.38±81.35	.000
	Patient	75	188.59±23.59	
CD4+ (after)	Control	13	196.77±54.24	.000
	Patient	75	388.33±34.42	

Viral load: copies/mm CD4+: cells/mm^3

Table No.2: Pearson Correlation

	Viral load (before)	Viral load (after)	CD4+ (before)	CD4+ (after)
Viral load (before)	1	-.560**	-.633**	.569**
		.000	.000	.000
Viral load (after)		1	.827**	-.678**
			.000	.000
CD4+ (before)			1	-.685**
				.000
CD4+ (after)				1

**. Correlation is significant at 0.01 level (2-tailed)

DISCUSSION

Bartlett et al., (2002)[3] reported that combination of two nucleoside reverse transcriptase inhibitor suppress HIV much better as compared with single NRTI. Popular nucleoside reverse transcriptase inhibitors in combination are tenovofir along with emtricitabline in resource rich regions. These two drugs are co formulated as a single drug and are advised once a day. Abacavir with lumividine is other combination but abacavir need sensitivity testing before administration. Mehandru (2004)[4] reported that combination antiretroviral therapy has a beneficial effect on laboratory markers of disease progression. Early treatment could decrease severity of acute disease; alter earlier viral set point, reduce rate of viral mutation, suppression of viral replication increase in immune function and reduce risk of viral transmission during high infectious stage of disease.

Zhou et al., (2010)[2] concluded that combination antiretroviral treatment increased CD4 level and decreased viral load in HIV1 Patient. They also stated that in order to get positive CD4 slope treatment need to start at early stage of disease. Auvert et al., (2005)[5] reported that antiretroviral therapy reduced HIV viral load in seminal fluid and cericovaginal secretions. They concluded that use of Zidovudine in HIV infected men decreased 50% risk of HIV transmission in their female sexual partners. Attia et al., (2009)[6] observed that there is no transmission of HIV in heterosexual patient with viral load below 400copies/ml and receiving antiretroviral therapy. They concluded that transmission can be reduced by 92% from 5.64 to 0.46 per 100 persons in patient on ART and non ART. Melbourne et al., (1999)[7] reported that best results against HIV can be achieved when patient take total prescribed antiretroviral doses at appropriate time. Those patients that take almost 90% doses but not at correct time, could not achieve successful treatment rate. The dose fluctuation was seen in 50% patients in early two months of treatment. The dose fluctuation was among those patients that took medicine within two hours of prescribed dose time and after two hours.

Kastrissios et al., (1998)[8] concluded that consequences of missed doses results in increasing viral load and development of mutant strains. As drug level fall below critical point, HAART inhibitory effect on viral replication may lessen, resulting in increased viral replication and viral load. Ariyoshi et al., (2000)[9] stated that HIV-2 infections are associated with lower plasma viral load and slower decline in CD4 count as compared to HIV-1 infections. However in short follow up treatment cases disease progress to advance stage. Mocroft et al., (2006)[10] concluded that CD4 level decreased significantly in HIV patients with viral load greater than 10,000copies/ml regardless of CART regimen used. Moreover response of CART was much better than of CART and NRTIS were better than NNRTIs. Single antiretroviral drug combination of two or more antiretroviral drug can suppress the HIV much better. They stated that combination ART achieves lifelong suppression of HIV replication but treatment is needed to continue for long duration. High cost of treatment in resource poor region limit the treatment rate and also control of HIV does not fully restore health in patient. Schapiro et al., (1999)[11] concluded that there are significant mutational drift in HIV and different patients are infected with different genotypes of HIV virus. Antiretroviral drug may eliminate the viral load but if resistance strains are present, they rapidly replace the eliminated viruses (Martinez et al., 2003)[12]. So it is better to advice combination antiretroviral therapy of three or four drugs from two different classes.

CONCLUSION

It can be concluded that ART is highly effective in AIDS patients with minimal adverse effects, makes the life of AIDS patients less miserable and improve the quality of life.

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Original Article

Treatment of Humeral Fracture

Current Pattern and Outcome of Closed Diaphyseal Humeral Fracture Treated With Intramedullary Interlocking Nail

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ABSTRACT

Objective: To determine the current pattern and outcome of the closed diaphyseal humeral fracture treated with intramedullary interlocking nail.

Study Design: Descriptive study

Place and Duration of Study: This study was carried out at Orthopedic Department of Liaquat University Hospital Hyderabad and PUMHS Benazirabad Nawabshah from March 2011 to February 2012.

Materials and methods: All the 40 patients with closed diaphyseal humeral shaft fracture between the ages 15-45 years were included in the study. All the patients after counseling and diagnosed as case with closed diaphyseal humeral shaft fracture on the basis of clinical examination and X-rays. Closed intramedullary nailing management procedure was used for closed diaphyseal humeral shaft fracture regarding with clinical presentation, preoperative findings and functional outcomes were documented including postoperative complications.

Results: Total 40 patients were selected in this study with humeral fracture. Male were found in majority. From types of fractures transverse fractures were most common 45% and road accidents were seen in majority. Most common complication was post operative pain in 40% of cases; Excellent results were found in the 55% of the cases while good in 20%, fair in 10% and 5% results were noted poor in the patients

Conclusion: In the conclusion of this study the closed intramedullary interlocking nailing procedure is the very good method for treatment of fracture shaft of humerus including with very good outcome.

Key Words: Intramedullary interlocking nail, diaphyseal humeral fracture

INTRODUCTION

Humeral fractures presents about 3% of all fractures.[1] About 30% of these injuries need to be treated surgically.[2] Humeral fractures mostly resulting of the direct force during impact, road traffic accidents and crush injuries. Indirect forces like fall on elbow side or extended arm or contractions of strong muscular, may produce the humeral fracture. The most frequent site of the fracture is between the middle and the distal third of the humerus.[3,4] Since of close anatomic assosiation among humerus and radial nerve, nerve injuries are common and mostly associated to spiral fractures. Occurrence of radial nerve injury is 6%–15% reasoned by this fractures.[5] Humeral uncomplicated fractures are frequently managed conservatively. Commonly operative methods used are the dynamic compression plate (DCP) and intramedullary nail for humeral fractures.[6,7] These procedures having clinically very good outcome. Nowadays these surgical procedures are used for the treatment of humeral fractures and also having some advantages and disadvantages mechanically and anatomicaly.[8] Visualization of plating with fixation, that's known as an exact anatomically decreases and defense of radial nerve, may decrease the chance of malunion but needs of large intraoperative exposure related to soft-tissue stripping.[8] Regular improvement in propose of IMN has guaranteed the clinical submission of intramedullary nail fixation in treatment of fractures of humeral shaft. Many reports suggested that IMN is standard surgical procedure.[9,10] Intramedullary nail having benefit of closed insertion procedures, whole periosteal blood supply, and load-sharing involuntary properties. The IMN can reduce the effects of stress shielding at the fracture site and lower the incidence of re-fracture after implant removal.[8] A major complication is the rotator cuff impairment of IMN, that's may lead to shoulder impingement and shoulder movement restriction. Iatrogenic damage of radial nerve throughout ante grade nailing is main problem during procedure.[8] Purpose of this study to determine the results of diaphyseal humeral fracture by closed Intramedullary nailing and whether it is safe and reliable method.

MATERIALS AND METHODS

This descriptive study was contains 40 patients and was carried out at Orthopedic Department of liaquat University Hospital Hyderabad and PUMHS Benazirabad Nawabshah with the duration of time March 2011 to February 2012. Both male and female were included in the study between the ages of 15 to 45

years. All the patients with closed diaphyseal humeral shaft fracture on the basis of clinical examination and X-rays were included in the study. All the patients after counseling for study and taking written consent were included in this study. All the cases with open fracture, associated with severe chest or abdominal injuries, pathological fractures and malunited fractures with neurological deficit were excluded from the study. In this study closed *intramedullary nailing* procedure used for closed diaphyseal humeral fracture. All the patients lying on supine position with head rotated to contra lateral side. Longitudinal incision 1-3 CM was done centered over tip of greater tuberiosity, AWL passed just medical to the tip of greater tuberiosity 0.5cm posterior to basipetal groove to make entry point, reaming of proximal mataphysis of humerus with diameter of 8mm approximately 0.4 cm was done, closed reduction had achieved according C-arm guidance and guide wire was passed. Nail length was measured with subtracting exposed guide wire from total length of the guide wire. With proper length and diameter nail was passed till its proximal end was beneath the bone by 0.5cm to avoid the sub a cromial impingement, after that guide wire was removed and proximal and distal locking was done. Figure 1.

Figure No.1:

On the 1st post-operative day extremity was elevated on a Thomas arm splint or by suspension with abduction and external rotation at shoulder. On 2nd postoperative day passive movement was start including pendular exercise and assisted full forward flexion with the limit of pain, Figure 2. and from 7th day overhead abduction, external rotation and internal rotations were begun.

Figure No.2:

On the follow-up weakly in 1st month, fortnightly in 2nd and 3rd month and monthly up to 1 year clinical and radiological analysis was performed. Preoperative presentation of fracture, operative findings and management outcomes were documented including with postoperative complications. Detailed Clinical examination of the patient along with all base line investigations were done and recorded in Performa. All the data was entered and analyzed in the SPSS program version 16.0 simple frequencies and percentages of the qualitative data were computed.

RESULTS

Total 40 patients with closed diaphyseal humeral shaft fracture were selected in this study, from all of them male found in majority 80% while female were noted 20%, mostly patients were documented in the age group of (15 to 45) years 50%, while 30% were in age group of (29 to 38) years and only 20% of the cases were found in the age group of (39-48) years of the age. Table 1.

Table. No. 1. Basic characteristics of the Patients. (n=40)

	Frequency	Parentage
Gender		
Male	32	80.0%
Female	08	20.0%
Age groups		
15-25	20	50.0%
26-35	12	30.0%
36-45	08	20.0%

Table. No. 2: Clinical pattern of the Patients. (n=40)

	Frequency	Parentage
Fracture location		
Left	22	55.0%
Right	16	40.0%
Bilateral	02	05.0%
Mode of injury		
Fall	08	20.0%
R.T.A	20	50.0%
Others	12	30.0%
Types of fracture		
Oblique	10	25.0%
Transverse	18	45.5%
Spirale	04	10.0%
Comminuted	06	15.0%
Location of fracture on humerus shaft		
Middle	22	55.0%
Proximal	14	30.0%
Lower	04	10.0%

On the clinical presentation fractures were found in majority at left side 55%, right side fractures were seen 40% and only 5% fractures were noted bilateral. Road

traffic accidents were found in 50% of the cases while falling patients 30% and 20% patients were comes with other different causes. According to types of fracture transverse fractures were seen most common 45%, Oblique fractures 25%, comminuted fractures 15% and patients with spiral fracture were 10%. Middle site fractures were seen 55% while 30% fractures were at proximal site. Table 2.

In this study most common complication was post operative severe pain in 40% of the cases and other complications as; Infection, Radial Nerve Palsy, Minimal Loss of Fixation, Delay union, Elbow stiffness and Shoulder stiffness 05.0%, 10.0%, 10.0%, 15.0% , 15.0% and 20.0% respectively. Table 3.

Excellent results were found in the 55% of the cases while good in 20%, fair in 10% and 5% results were noted poor in the patients. Table 4.

Table No. 3: Postoperative complications of the patients. N=40

Complications	Frequency	%age
Post operative severe pain	16	40.0%
Infection	02	05.0%
Radial Nerve Palsy	04	10.0%
Minimal Loss of Fixation	04	10.0%
Delay union	06	15.0%
Elbow stiffness	06	15.0%
Shoulder stiffness	08	20.0%

Table No.4: Outcome n=40

Results	No. of cases/%age
Excellent	22/(55.0%)
Good	12/(20.0%)
Fair	4/(10.0%)
Poor	2/(5.0%)

DISCUSSION

Femoral fractures are the very common fractures thats orthopaedic surgeons encounter, because that's fractures most often result due to high energy trauma, these are often related to concomitant injuries of internal organs. Femoral fractures resulting from the drawbacks of fast lifestyle and violence and these are main risks for mortality and morbidity in the cases with that's injury.[11,12] In the study of Zulfiqar et al reported that male were in majprity as compare to females, and most common age group of 20 – 30 years.[13] Johnson and Greenberg[14] also reported majority of males. Similarly in the present study male found in majority 75% while female were noted 25%, and mostly patients were documented in the age group of (15 to 25) years 50%, while 30% were in age group of (26 to 35) years and only 20% of the cases were found in the age group of (36-45) years of the age.

Crates et al, reported that majority of males in the study of acute humeral shaft fractures.[15]

Road traffic accident is the most common mode of injury in different studies a; in the study of Rommens et al[16] he reported that from 39 patients, 21 was with the history of road traffic accident. In the study of Tingstad,[17] reported that road traffic accident was most common mode of injury. Similarly in this study fractures were found in majority at left side 55%, right side fractures were seen 40% and only 5% fractures were noted bilateral. Road traffic accidents were found in 50% of the cases while falling patients 30% and 20% patients were comes with other different causes.

In the study of Marya KM et al[18] shows that middle third fractures of the forearm bones were 52 %. According to the Manjappa CN et al[19] 60% cases were with middle third region of diaphyseal fracture, 25 % case were with proximal third fracture and 15% cases had lower third fracture. As well as in present study transverse fractures were seen most common 45%, Oblique fractures 25%, comminuted fractures 15% and patients with spiral fracture were 10%. Middle site fractures were seen 55% while 30% fractures were at proximal site.

In the study of Erwin DENIES et al, reported complications in the patients those treated with intramedullary interlocking nailing method the radial nerve palsy 4.1%, hardware failure 8.1% and infections was 2.0%.[20] In this study most common complication was found as post operative severe pain in 40% of the cases and other complications as; Infection, Radial Nerve Palsy, Minimal Loss of Fixation, Delay union, Elbow stiffness and Shoulder stiffness 05.0%, 10.0%, 10.0%, 15.0% , 15.0% and 20.0% respectively

Excellent results were found in the 55% of the cases while good in 20%, fair in 10% and 5% results were noted poor in the patients. While in the study of Mohammad Naeem-Ur-Razaq reported that fracture union rate achieved at 32 weeks after the surgery was 97.83% while 34.04% cases had delayed union of the fracture.[21] In the above mentioned study of Zulfiqar et al,[13] mentioned that very excellent results 88% in the patients. There are many other studies reported very good results of IM interlocking in humeral fracture as; Deepah MK et al,[22] 92%, Klaus WK et al, [23] 91% and Solooki S et al, [24] showed excellent results in 94% of the patients.

CONCLUSION

On the basis of above mentioned observations in this study following conclusions can be made. Closed humeral interlocking nailing for diaphyseal humeral fracture gives good results and this is reliable secure fixation provides early postoperative rehabilitation both physically and psychologically with few complications.

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Original Article

Pancreatitis

To Determine the Frequency of Raised C-Reactive Protein in Patients of Acute Pancreatitis

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ABSTRACT

Objective: To determine the frequency of raised c-reactive protein in patients of acute pancreatitis.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at Surgical Department Jinnah Post Graduate Medical Centre Karachi and Dow University Hospital from January 2013 to June 2014.

Materials and Methods: The patients were selected on the basis of clinical features. Take detailed history regarding epigastric and upper abdomen pain. All the patients of either gender with acute abdominal pain presenting to emergency and diagnosed as acute pancreatitis by serum amylase of 1000 units or more were included in the study. Ranson Scoring and C reactive protein levels on admission were noted.

Results: A total of 144 patients, both males and females were included in the study. 17(11.80%) out of 144 subjects were males and rest were females 127(88.19%) cases. The minimum age was 25 years and maximum was 60 years but most of the patients were in the range of 40 to 55 years means age was 43±6.7 years. The minimum value was found to be 25 mg/L while maximum was 57 mg/L. Mean CRP was found to be 32.2± 11.43 mg/L for that group of patients. All the patients were also categorized as mild and moderate to severe on the basis of Ranson's criteria. 73% patients were found to have mild disease with rest having moderate to severe disease. Frequency of CRP observed in our study were in 139(96.52%) cases.

Conclusion: We concluded that C reactive protein was a useful severity assessment marker in patients with acute pancreatitis and it can be proposed as an important single factor for determining severity of patients presenting with acute pancreatitis.

Key Words: Ranson Criteria, Acute Pancreatitis, C-Reactive Protein

INTRODUCTION

Acute pancreatitis is acute inflammation of pancreas, a gland that serves many important functions, most common causes being gallstones and alcoholism. It is mostly a self limiting mild disease.[1] But some patients can develop severe pancreatitis with high mortality.[2]. About two third of the patients of acute pancreatitis have mild disease with 1% mortality. One third of the patients of acute pancreatitis have moderate to severe disease with around 30% mortality. The prevalence of acute pancreatitis in U.S is 0.04%[3], which is one of the highest in the world[4] and is rising[5].The prevalence of acute pancreatitis in Pakistan is 0.03%.The hospital admission rate for acute pancreatitis is 9.8 per year per 100 000 population in U.K ,although the annual incidence worldwide may vary from 5 to 50 per 100 000.The disease may occur at any age but there is a peak incidence in young women and older men. It is definitely one of the most common causes of acute abdominal pain requiring admission. Improved outcome in acute severe pancreatitis depends on early identification and rapid therapeutic interventions[6-7].Many scoring systems are used for this purpose like Ranson and APACHE but they are difficult to use due to their multifactorial nature. A number of unifactorial prognostic indices have been developed in routine clinical practice like c-reactive protein which is an acute phase reactant synthesized by hepatocytes and according to some studies is raised in about 23% of patients suffering from acute pancreatitis[8].Normally range of C-reactive protein in blood is 0-10 mg/ml. Serial measurement of C reactive protein is a simple way to predict severity. Another study highlighted the importance of unifactor in this regard.[9]. Acute pancreatitis is a disease that can result in multiple disasters like systemic inflammatory response, sepsis, multiorgan failure, and death. The severity of the inflammation, hemorrhage, or necrosis of the pancreas, peripancreatic fluid collection, or abscess are closely related with prognosis [9-10]. Bile reflux into the common bile duct and obstruction of the Ampulla Vater by biliary sludge or stone are supposed to cause biliary pancreatitis[11]. The obstruction of the common bile duct and the pancreatic duct separately or together may effect the resolution of the pancreatitis. Also transient or permanent obstruction, acute or chronic obstruction, and type of obstruction (like tumor

or stone, etc.) of these ducts are effective on the prognosis and determine the management. If the obstruction persists more than 48 hours, the complications increase [12]. The stones in the distal common bile duct and the pancreatic duct could not be detected in all patients with biliary pancreatitis.

MATERIALS AND METHODS

This is Cross sectional study conducted at at Surgical Department Jinnah Post Graduate Medical Centre Karachi and Dow University Hospital from January 2013 to June 2014.

The patients were selected on the basis of clinical features. Take detailed history regarding epigastric and upper abdomen pain. All the patients of either gender with acute abdominal pain presenting to emergency and diagnosed as acute pancreatitis by serum amylase of 1000 units or more were included in the study. Ranson Scoring and C reactive protein levels on admission were noted.

RESULTS

A total of 144 patients, both males and females were included in the study. 17(11.80%) out of 144 subjects were males and rest were females 127(88.19%) cases (Chart No.1). The minimum age was 25 years and maximum was 60 years but most of the patients were in the range of 40 to 55 years means age was 43±6.7 years (Chart No.2).

In this study single measurement of CRP was done at admission. The minimum value was found to be 25 mg/L while maximum was 57 mg/L. Mean CRP was foud to be 32.2± 11.43 mg/L for that group of patients. All the patients were also categorized as mild and moderate to severe on the basis of Ranson's criteria. 73% patients were found to have mild disease with rest having moderate to severe disease. Frequency of CRP observed in our study were in 139(96.52%) cases (Chart No.3)

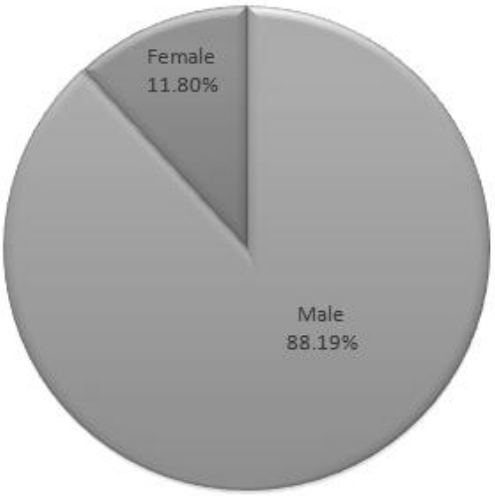

Chart No.1: Gender Distribution

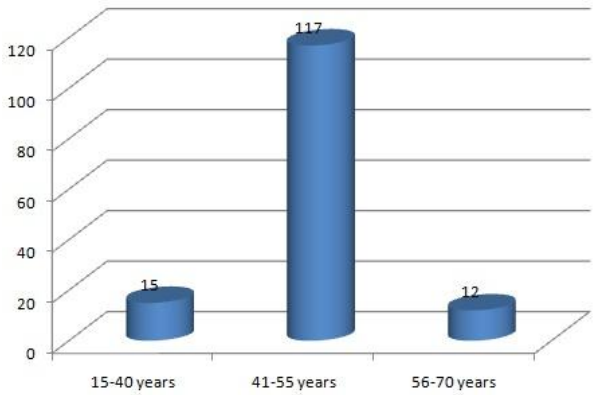

Chart No.2: Age Distribution

Chart No.3: Frequency of raised CRP

DISCUSSION

Acute pancreatitis is a disease effecting a wide range of population worldwide[13]. Regardless of etiology, it has been observed that the disease has significant complications. Although the mortality due to acute pancreatitis has decreased markedly in recent years, it is still a life- threatening disease. The demographic characteristics of acute pancreatitis are similar in many series; most patients are in the 50-60 year age group[14]. In most series published in the English literature, gallstones are the leading cause, followed by alcohol[15].The case is similar in our part of world where acute biliary pancreatitis supersedes all other causes of the disease and effects mainly middle age adults with about 80 percent cases falling in the age range of 30-50 years. The term idiopathic pancreatitis also exists but is much less diagnosed now due to more detailed investigations now being done to determine the etiology of acute pancreatitis. The frequency is lower in centers that perform extensive investigations and usually biliary causes are revealed. Accordingly, with the introduction of ERCP, the frequency has decreased from 30% to 20% in most centers[16].Other cause of pancreatitis although relatively uncommon are much important because delay in evaluating those causes and in turn failure to treat can lead to significant mortality.

Once a patient of acute abdominal pain presents to the emergency and suspicion of acute pancreatitis is high,

serum amylase or lipase levels should be send and an ultrasound examination ordered. If the suspicion of pancreatitis comes out to be true after these investigations and ultrasound confirming gallstones as the cause, then the most important question arises that what wil be the prognosis of our patient. It is really critical to determine whether we are dealing with a patient of mild pancreatitis with almost no mortality or on the other hand patient of moderate to severe pancreatitis with significant mortality. How can prognosis of acute pancreatitis be determined and there are multiple simple answers to it. There are multiple scoring systems for past century in use to evaluate the severity of pancreatitis. The most widely and trustfully used is the famous Ranson's criteria[17] but it is not the only one. Other scoring systems like APACHE 2, Glasgow scoring etc are also used. CTSI (CT scan severity index) has also been used for years[18] .A problem common to all the scoring systems is that these involve multiple factors assessment which is quite troublesome. The main issues with the Ranson criteria score are the need to wait 48 hours to confirm whether a patient should be considered critically ill and the fact that it does not allow for scores to be reevaluated on a daily basis. The APACHE II is commonly used in intensive care units and permits a daily score to be calculated as needed. However, it also presents problems, such as the complexity of calculating the score, the age factor and difficulty in distinguishing between necrotizing and interstitial pancreatitis as well as between infected and sterile necrotizing pancreatitis[19]. In addition, APACHE II can overestimate the severity of acute pancreatitis, characterizing as critical some patients who do not actually have organ failure. For this reason, other criteria, such as the Sepsis-related Organ Failure Assessment (SOFA) and Marshall scores, have been suggested in recent years for evaluating patients with severe acute pancreatitis[20].

Now remains the last but the most researched prognostic index that is a single factor assessment for determining prognosis of acute pancreatitis. There can be two type of single factors which can be used to determine the prognosis. They can either be clinical factor or a lab index. Clinical factors indicating a severe disease include fluid sequesteration, a raised hematocrit count of above 47 at admission or features of SIRS, All these are now accepted as single factor to indicate high mortality.

Recent studies have suggested that the serum levels of interleukins and TNF-α may be used to identify patients who are prone to develop local or systemic complications and were compared with CRP which has been employed in the prediction of severity of acute pancreatitis [21,22]. Early identification of such patients can lead to a more intensive management that would result to a decreased morbidity and mortality of that potentially fatal disease .In our study, the frequency of raised CRP in pancreatitis was found out. CRP is an acute phase reactant synthesized by hepatocytes and is considered to be the most important single prognostic factor in determining prognostic of acute pancreatitis. It is not specific for pancreatitis and is raised in a variety of of inflammatory conditions. Our study results showed that all patients with acute pancreatitis had raised values and in addition patients who were found to have severe disease according to Ranson's criteria also had substantially increased CRP levels. This finding indicates that CRP levels directly correlate with the severity of pancreatitis to some extent. Previously multiple studies have been done to evaluate the prognostic value of CRP and had almost similar results. One study stated that if on admission, CRP is found to be normal or mildly raised, then severe pancreatitis is very unlikely and can be confidently excluded[23].Our study results also supported this fact and also showed a strong correlation between severity on Ranson's scoring and on CRP. Another study done by Gorunet and his colleagues in 2010 estimated multiple factors to detect the severity of acute pancreatitis that included Ranson's scoring, CRP and other serum biochemical markers. The study concluded that CRP is an independent factor in assessing the prognosis of acute pancreatitis[24]. After studying the research protocol in detail, readers will have a strong idea on how important CRP estimation is and how helpful its assessment can be to evaluate the severity of pancreatitis.

CONCLUSION

Acute pancreatitis is a major causes of disease specific morbidity and mortality in Pakistan. The diagnosis of acute pancreatitis is principally clinical supported by hematology and radiolology. Although no age is exempted from this disease but patients aged between 30 to 50 years are mostly at risk. In our setup patients presenting to the emergency with abdominal pain are usually diagnosed clinically confirmed by raised serum amylase and then prognosis assessed by Ranson scoring usually.In our study of assessing the frequency of raised c reactive protein in acute pancreatitis.CRP came out to be a very good prognostic marker.

Recommendations: On the basis of our study ,we can recommend CRP to be measured in all patients of acute pancreatitis and we also recommend an analytical study to prove the prognostic value of CRP.

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Original Article

GBS and AFP

GBS and AFP (Acute flaccid Paralysis) System in AJK

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ABSTRACT

Objective: Main objective of the study is to highlight the major cause of AFP and % of GBS represents the AFP during the study period.

Study Design: Retrospective analytical study.

Place and Duration of Study: This study was conducted in AJK, for the duration of three years from January 2011 to December 2013.

Materials and Methods: Retrospective analysis of AFP cases reported during 2011-2013. Primarily the AFP cases investigated through history and clinical examination. Principal cause of AFP (Acute flaccid Paralysis) cases were investigated through specific tests like serum electrolytes, CSF (cerebrospinal fluid), electromyogram and viral culture from stool sample to exclude poliovirus. All the cases reported from AJK and taken on the line list labelling as GBS were included in the study during 2011-2013.

Results: Three years data analysis shows more than 50% GBS cases presenting AFP and the numbers are increasing every year. Most of the GBS and even AFP belong to 6-59 months age group. More than 55% GBS cases recover completely and this proportion increased from 2011-2013.

Conclusion: Data analysis revealed GBS is a major cause of AFP in AJK and needs not to be overlooked to keep poliovirus transmission ceased here. AFP surveillance system is huge resource and this is a high time to study all the causes responsible for acute flaccid paralysis to strengthen polio eradication efforts and to develop understanding for prevention and control, to avoid acute flaccid paralysis related morbidity and mortality amongst children in Pakistan.

Key Words: GBS, Guillain Barre Syndrome AFP Surveillance, Polio.

INTRODUCTION

Conditions presenting with AFP can be grouped into 2 categories .Conditions always presenting with AFP like, Paralytic poliomyelitis, GBS (Guillain Barre syndrome), Transversmyelitis, Traumatic neuritis and conditions sometime presenting with AFP like, Muscle hypotonia, Hypokalemic paralysis, POTTs disease, TB Meningitis, Osteomyelitis. This study mainly focuses on GBS which seems the foremost cause of AFP in AJK.

Polio is the priority operation of WHO in Pakistan because the situation study revealed, Pakistan, Cameroon and Syria pretence bigger risk of Poliovirus export globally[1]. The end of 2013 brought >99% decrease in Polio case burden since 1988 but three endemic countries Pakistan, Nigeria and Afghanistan has failed to interrupt virus transmission yet[2].

To eradicate Polio from Pakistan AFP surveillance was one of the four prong approach adopted.AFP (acute flaccid paralysis) is a group of sign and symptoms which are similar to Poliovirus infection[3]. AFP surveillance strategy was adopted to identify all the AFP cases and stool sample of all AFP cases tested to exclude poliovirus[4].

Polio generally presents with asymmetrical paralysis while AFP surveillance system also include infections presenting symmetrical paralysis. Unfortunately clinical picture of Polio is not typical, it sometimes present like other neurological diseases as GBS (Guillain- Barre Syndrome). That's the reason definitive diagnosis cannot be made through serological testing and viral culture from stools specimen is considered to be the golden rule to exclude poliovirus[5].

Conditions presenting with AFP can be grouped into 2 categories .Conditions always presenting with AFP like, Paralytic poliomyelitis, GBS (Guillain Barre syndrome), Transversmyelitis, Traumatic neuritis and conditions sometime presenting with AFP like, Muscle hypotonia, Hypokalemic paralysis, POTTs disease, TB Meningitis, Osteomyelitis.

This study mainly focuses on GBS which appear the foremost cause of AFP[6] and remain a common cause of AFP after eradication of Polio in many countries[7,8,9]. Number of studies show frequency of GBS is 5-5/100000 children/year globally[10,11,12]. GBS is an acute demyelinising poly neuropathy measured by the ascending symmetrical flaccid paralysis, on careful examination DTR (deep tendon reflex) are either absent or decreased. In addition to flaccid paralysis patient may experience sensory symptoms and involve cranial

nerves, respiratory muscles and autonomic nervous system may also affect in GBS. GBS with axonal involvement is more severe than demyelinating type, diagnosis of the disease is mostly on clinical grounds in addition to this CSF (Cerebrospinal fluid) examination, electrophysiological testing, EMG (Electromyography), NCS (Nerve conduction study) are essentials to confirm the diagnosis.

GBS was discovered by three French neurologists in 1916, Georges Guilain, Jean-Alexendre Barre and Andre Strohl[13]. Principally there are three subtypes of GBS, AIDP (acute inflammatory demyelinating polyradiculoneuropathy), AMAN (acute motor axonal neuropathy) and AMSAN (acute motor and sensory axonal neuropathy).The most common subtype is AIDP this is syndrome[14], AMAN is characterized by the neurological deficit based on motor defect[15] and AMSAN involve both motor and sensory axonal defect[16]. C. Millar Fisher in 1956 described Ataxia, Areflexia and Opthalmoplegia now known as Miller Fisher, another important variant of GBS.[17]

Management of the disease includes supportive treatment, frequent monitoring, and maintenance of airway and ventilator support when indicated, feeding, bladder and bowl management. Specific treatment included intravenous immunoglobulin (IVIG) have magical effect beside plasmaphresis. Prognosis and recovery is good in 95% of cases but it takes weeks to months[18].

MATERIALS AND METHODS

Retrospective analysis of AFP cases reported during 2013-2011.Primarily the AFP cases investigated through history and clinical examination and principal cause of AFP (Acute flaccid Paralysis) cases was investigated through specific tests like serum electrolytes, CSF (cerebrospinal fluid), electromyogram and viral culture from stool sample to exclude poliovirus. Efforts were made during the study to analyse what % of GBS represents the AFP during the study period and seasonal trend of GBS was identified using time series. All the cases reported from AJK and taken on the line list labelling as GBS were included in the study during 2013-2011.

RESULTS

Data consideration: Numbers rounded off for calculation purposes.

Proportion of the GBS presenting AFP: 32/50 (64%), 23/34(67.7%) and 21/45 (46.7%) GBS (Gillian Barre syndrome) presenting AFP (Acute Flaccid paralysis) cases respectively in 2013, 2012, and 2011.Data analysis in table also revealed 28/50(88%), 21/34 (91%), 18/45(86%) of GBS cases presented with symmetrical paralysis follow by fever in 63%,70% and 57% in GBS cases during 2013,2012 and 2011 respectively (Table 1).

Age: 37/50 (74%), 24/34 (71%) and 26/45 (58%) AFP cases belong to 6- 59 months age category during 2013, 2012 and 2011 respectively and same was the picture revealed by the data analysis (table 2) for GBS, 25/32 (78.1%),14/23 (61%) and 11/21(52%) of GBS cases belongs to 6-59 months age group.

Immunization status: Data analysis shows all the cases having age matched OPV doses in both routine EPI and SIAs (Special Immunization Activities). Cases reported in 2013 having 27 months median age and received 10 median OPV doses while 81% cases received 3 routine EPI doses of OPV. While 36 months median age and 10 median OPV doses while 83% of cases received 3 OPV doses through routine EPI, 48 months median age and having 9 OPV doses while 68% of the cases having 3 OPV doses through routine EPI during 2012 and 2011 respectively.

Table No.1: Shows year wise % of GBS presenting AFP and clinical feature of cases during study period 2011-2013.

Year	AFP	GBS		Asym:				Fever			
	n	n	%	Yes		No		Yes		No	
				n	%	n	%	n	%	n	%
2013	50	32	64.0	4	13	28	88	20	63	12	37
2012	34	23	67.6	2	8.7	21	91	16	70	7	30
2011	45	21	46.7	3	14	18	86	12	57	9	43

Table No.2: Age wise distribution of GBS presenting AFP

Year	0-5				6-59				60+				Accumulative	
	AFP		GBS		AFP		GBS		AFP		GBS		AFP	GBS
	n	%	n	%	n	%	n	%	n	%	n	%		
2013	0	0	0	0	37	74	25	78.1	13	26	7	21.9	50	32
2012	0	0	0	0	24	70.6	14	60.9	10	29.4	9	39.1	34	23
2011	1	2.2	1	4.76	26	57.8	11	52.4	18	40	9	42.9	45	21

Table No.3: Shows distribution of median age and additional OPV doses in GBS during 2011-2013

Year	GBS	Median age	Median SIA OPV	Routine OPV doses
2013	32	27	10	81
2012	23	36	10	83
2011	21	48	9	68

Table No.4: Distribution of GBS cases according to clinical outcome 60 days follow up during 2011-2013

Year	GBS	Residual weakness				Died	
		yes		No			
		n	%	n	%	n	%
2013	32	8	25	23	71.9	1	3.1
2012	23	7	30	14	60.9	2	8.7
2011	21	7	33	12	57.1	2	9.5

Clinical outcome of the GBS: On follow up examination after 60 days from onset of paralysis 23/32 (72%), 14/23(61%) and 12/21 (57%) had no residual weakness whereas 1/32 (3%),2/23(9%) and 2/21 (9.5%) patients died in 2013,2012 and 2011 respectively.

Seasonal Trend in GBS cases: There was no significant seasonal trend for GBS stirring found during the study period apart from a considerable increase in GBS cases 32, 23 and 21 from 2013, 2012 and 2011 respectively.

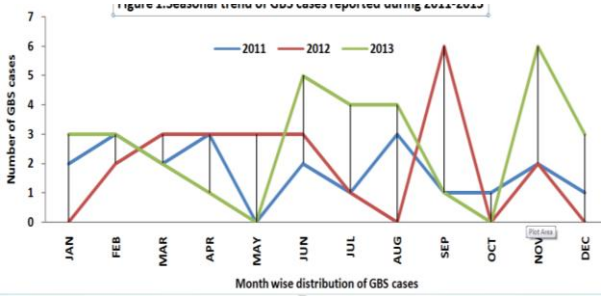

Figure No.1: Seasonal trend of GBS cases reported during 2011-2013

DISCUSSION

Pakistan appearing to be the last country to eradicate Polio and major global case burden is reported from Pakistan. Country failure to interrupt transmission of poliovirus poses threats of poliovirus export to many countries. Numbers of cases reported and districts/areas infected this year are high among last five year. There are number of district which has not reported a wild polio case through the AFP surveillance system but the positive environmental sample shows presence of poliovirus. Number of AFP cases reported annually decreasing throughout the country. All the issues collectively hampering the polio eradication progress in Pakistan.

During this study data analysed retrospectively to identify the major contributor of AFP and efforts were made to develop an understanding between causes of AFP and AFP surveillance system in AJK. Field experience of AFP surveillance system in AJK shows many doctors believe that polio is the only cause of AFP, resulted a sharp decline of AFP cases in AJK.

Data analysis revealed GBS is a major cause of AFP in AJK and needs not to be overlooked to keep poliovirus transmission ceased here. GBS causes 64% of AFP cases in 2013 similarly 67% and 47% in 2012 and 2011 respectively. More than 80% of GBS cases presented with symmetrical paralysis/weakness. More than 72% of GBS patients fully recovered when examined after 2 months of the paralysis/weakness started in cases reported during the year 2013, while 61% in 2012 and 57% in 2011 fully recovered within 2 months after paralysis/weakness started. There was no significant seasonal trend found in GBS infection during the study period in AJK.

CONCLUSION

AFP surveillance system in Pakistan is based on sensitivity more than specificity is a daring for not to miss any poliovirus circulation in the country. AFP surveillance system is huge resource and this is a high time to study all the factors responsible for acute flaccid paralysis to strengthen polio eradication efforts and to know more about how to avoid morbidity and mortality related to AFP in Pakistan.

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Original Article

Sensitivity of Micro-Organism

Frequency and Sensitivity of Micro-Organism in Post-Operative Wound Infections: A Quest for Microbes

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ABSTRACT

Objective: To determine the frequency of common organisms involved in post- operative wound infection. To determine the sensitivity of micro-organism for different antibiotics.

Study Design: prospective cross-sectional descriptive study.

Place and Duration of Study: This study was conducted in 3 Surgical Units of Civil Hospital Karachi from April to September 2010.

Materials and Methods: 72 swab samples were collected from patients who had undergone operations in 3 Surgical Units of Civil Hospital Karachi during a period of 6 month from April to September, 2010. Samples were obtained from the hospital and processed in Civil hospital Karachi lab (Microbiology Department).

Results: Out of 72 bacterial isolates found in post-operative wound infection, 30 (41.66%) were E.Coli, followed by Klebsiella species 14 (19.44%), pseudomonas aeruginosa 13 (1.38%), staphylococcus aureus 6 (9.72%), providentia species 1 (1.38%), proteus mirabilis 1 (1.38%), Actinobacter 1 (1.38%) and no growth 6 (9.72%). The result showed that the occurrence of infection was higher in the age group between 20 -40 than any other group. There is no significant difference between male and female sexes in the occurrence of infection. Infection was more in the operation done under emergency circumstance than the elective ones. There was no significant association between infection, and co-morbidities and past history of wound infection. The sensitivity pattern of 4 main bacteria, Frequently found in the study i.e. E.coli, klebsiella, pseudomonas aeruginosa and s.aureus isolates, suggested that the organisms was more sensitive to imipenem, Amikacin sulphate, Ceftazidime, Cefperazone/Sulbactum and Pipercillin/Tazobactum than other groups of drugs.

Conclusion: The most causative organism was E.coli, infection higher among the patients operated in emergency and imipenem, Amikacin sulphate were found to be more sensitive.

Key Words: post-operative, wound infection, sensitivity, antibiotics

INTRODUCTION

Infection is one of the leading causes that are responsible for high percentage of morbidity and mortality in surgical patients. Infection of a wound may be defined as invasion of organism through tissues following a breakdown of local and systemic host defenses[1].

post-operative wound infection after surgical operation may originate during the operation (primary wound infection) or may occur after the operation from sources in the ward or as a result of some complication (secondary wound infection)[2]. Wound infections are the commonest and most troublesome disorder of wound healing[3].

The introduction of antibiotics/antimicrobials and antiseptic techniques are considered to be an important and valuable success on the path leading to safe surgery. The antimicrobial agents also enable us to perform in many conditions that were thought to be unavoidable and impossible in the era that lacked the factors of antibiotics and antiseptics.[4]The discovery of effective antibiotics and the adoption of antiseptic techniques and measures has been an important milestone in order to prevent infections. Even with all the development and advancement, post-operative wound infection have not been eliminated and is still a burning issue in Pakistan like certain other developing and also developed countries.

Wound infections after contaminated operations are usually caused by normal bacterial flora on the opened and incised mucus membranes. [4, 5]

Infection in a wound is basically a manifestation of unbalanced see-saw played between host and bacteria in which the plank leans on the bacterial equilibrium is in favor of bacteria.[6]

The absolute prevention of surgical wound infections seems to be an impossible goal. Nosocomial infection is the second commonest cause of post-operative wound infection[7] and cause discomfort, prolonged hospital stay, more day off work and increment cost of therapy for the patient.[8]

This study has been designed to determine the different factors and variables that have impact on producing post-operative wound infection and to analyze the antimicrobial sensitivity of commonly used antibiotics in the hospital.

MATERIALS AND METHODS

This is a prospective cross-sectional descriptive study conducted in 3 surgical units of Civil hospital Karachi from April to September 2010. Each surgical unit is a 40 bedded unit with admitting once a week.

All patients of more than 12 years of age were admitted. All patients with surgical site infection or a discharging wound post-operatively were included. Wound infection developed within 25 days of surgery were included. Wound infection was diagnosed and labeled with the presence of at least one of the signs and symptoms of infection i.e. fever, itching, pain and soreness, purulence and localized swelling around the area of wound, a rising a total leukocyte count and bacterial growth on blood cultures.

Patients not giving an informed consent, or having a wound infection but not have been operated in Civil hospital Karachi were excluded.

A pretested questionnaire was used to enter the information which included age, gender, co-morbid conditions such as diabetes mellitus, hypertension, tuberculosis etc., past history of wound infection, type of surgery, characteristics of wounds and organisms isolated with antibiotic sensitivity were recorded.

The statistics were reported after calculation by SPSS version 17.0 version on computer.

The specimens of pus were collected from the patients by following the aseptic techniques with sterile cotton wool swab.

Several media and tests were used for the isolation, identification and testing the susceptibility of the isolates for common used antibiotics. The media used were Blood agar, MsConkey agar, chocolate agar, nutrient agar, Mannitol salt agar, Simmons citrate agar, kligler iron agar, Mueller-Hinton agar Sulfide formation indole production, motility test, thioglycollate broth, coagulase, catalase, urease, oxidase tests.

After overnight incubation (37^0 C in ambient air 16-18 hours; upto 24 hours), the culture plates were examined for growth. Identification was performed both microscopically and macroscopically by using standard biochemical techniques.

RESULTS

A total of 72 samples were obtained from the patients of 3 general surgery units suffering from the post-operative wound infection and the specimens were sent to the microbiology lab for culture and sensitivity report. The most common surgical procedure was exploratory laprotomy, followed by appendectomies.

The age groups were divided into 3 categories as shown in table-1. Majority patients (48.6%) were between 12-31 years of age. Gender distribution was almost equal. There were 37 (51.3%) males.

Fifty six (77.7%) patients with wound infection did not have any co- morbidities while 16 (22.2%) had co-morbidities. Out of these 16 patients, 9 had diabetes mellitus, 5 had hypertension, one had hepatitis C, 2 patients had hepatitis B and 2 had tuberculosis.

Out of 72, 67 (93.05%) had no past history of wound infection. Among the 72 surgeries which developed post operative wound infection, 26 (36.11%) were elective surgeries and 46 (63.88%) were emergency surgeries.

Table No.1: Age Distribution

Age	Frequency (%)	Percent
12-31	35 (48.6)	48.6
32-51	28 (38.8)	13.88
52-71	9 (12.5)	5.55
Total	72	100.0

Table No.2: Sensitivity Pattern of Micro-Organism for Different Antibiotics

Antibiotics	Micro-organisms			
	E.coli (n=30)	Klebsiella Species (n=14)	Pseudomonas aeruginosa (n=13)	Staphylococcus aureus (n=6)
Imipenem	20	8	10	5
Amikacin	16	17	5	3
Augmentin	0	0	0	5
Ceftazidime	15	7	1	1
Oflaxacin	3	5	0	2
Sparfloxacin	5	5	7	2
Cefperazone/Sulbactum	19	9	13	0
Ceftizoxime	9	7	0	1
Ciprofloxacin	5	5	3	2
Pipercillin/Tozabactum	13	4	9	0
Ceftriaxone	2	1	3	1

The most common causative organism was Escherichia coli 30 (41.66%), followed by by Klebsiella species 14 (19.44%), Pseudomonas areuginosa 13 (1.38%), Staphylococcus aureus 6 (9.72%), providentia species 1 (1.38%), proteus mirabilis 1 (1.38%), Actinobacter 1 (1.38%) and no growth 6 (9.72%). Organism sensitivities is shown in table-2.

Following drugs are used as prophylaxis due to easy availability and economic conditions of our patients. Ceftriaxone, Amoxicillin clavulanate, Ciprofloxacin, Gentamycin and Metronidazole are given. This study shows that Imipenem and Amikacin were the most sensitive antibiotics.

DISCUSSION

Our study found E. Coli to be the commonest causative organism followed by Klebsiella, pseudomonas and staphlococcus respectively. Similarly study conducted on 200 patients in Islamabad showed 70 (30%) were e.coli, followed by klebsiella species 50 (25%), cloacae 30 (15%) and proteus mirabilis 20 (10%). Infection was found to be most common among age group b/w 50-60 years.[9] While another study conducted in the same hospital on 11 patients found Staph. aureus as the commonest organism followed by E. coli, streptococcus and Pseudomonas.

According to study held in civil hospital Karachi, Pakistan (Dow university of health sciences) in the year 2006; out of 11 infection wounds. 5(45.5%) were S.aureus, followed by E.Coli 3 (27.7%), S.pyogens 1(9.1%), E.coli and pseudomonas asruginosa 2 (18.2%).[10]

A study conducted in Hyderabad on 112 infected wounds, found E. Coli to be the commonest organism followed by klebsiella species and staphylococcus epidermidis.[11] Penicillin derivatives (pipercillin and tazobactum) and Carbapenem (imipenem and meropenem) were the most sensitive antibiotics covering all the organism isolated in this study. Cephalosporins were found to be ineffective against the common pathogens.[11] In contrast our study found that Imipenem and Amikacin sulphate were the most sensitive antibiotics.

In Nigeria 60 infected wounds were examined, in 20 (33.3%) patients pseudomonas was isolated followed by staphylococcus aureus 13 (21.7%), klebsiella species 10 (16.7%).[12] According to study held in Jordan conducted on 115 infected wound, 20 (27.8%) were pseudomonas, aeruginosa, Ecoli 18 (15.6%) and , staphylococcus aureus 17 (14.7%) and 15 (13%) Acinetobacter calcoaceticus.[13]

In Mymensingh Medical College Hospital, total 74 clinical sample were taken. Bacterial growth was yielded in 43 samples and the distribution of isolates was as follows: Pseudomonas spp 16, Esch.coli 13, Staphylococcus aureus 08, Klebsiella spp. 03 and others 03. All the Esch.coli and Klebsiella isolates were resistant to amoxicillin.[14] Ceftriaxone (65.6% and 100% respectively) and ciprofloxacin (71.4% and 100%) still appeared to be highly sensitive for both species. Over 93% strains of Pseudomonas were sensitive to Ceftazidime and aztreonam. Whereas, 100% of those strains were sensitive to cloxacillin. Over 50% of all isolates were sensitive to gentamicin but resistant to cefalexin and cotrimoxazole.[14]

In another study 516 bacterial isolates were obtained from 502 pus samples, collected from post operative wound infections. Staphylococcus aureus was the most frequently isolated bacteria followed by Escherichia coli than Pseudomonas aeruginosa and Klebsiella pneumoniae. Majority of the isolates were resistant to ampicillin, ampicillin-clavulanic acid, cefuroxime, cefotaxime, fluoroquinolones and cotrimoxazole.[15]

CONCLUSION

This study concludes that despite of modern Surgical and antiseptic techniques and prophylactic use of antibiotics, post-operative wound infection is still a major contributory factor of patient's morbidity. E.coli was found to be the most common causative organism. Type of surgery (elective and emergency) was an important factor.

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Original Article

AFP Surveillance

Evaluation of AFP Surveillance Sensitivity in AJK

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ABSTRACT

Objective: Main objective of the study is to analyse sensitivity of the surveillance system, required to keep poliovirus circulation ceased in AJK.

Study Design: Retrospective analysis of AFP cases reported during the study period.

Place and Duration of Study: This study included all the AFP cases reported during the study period in AJK from Jan. 2011 to Dec. 2013.

Materials and Methods: Historical data is used to analyse AFP surveillance for detecting poliovirus infection in children age <15 years in the study area based on few assumptions that all the results are negative and adequate information were available to make ultimate diagnosis of each AFP case reported in the area during study period. Surveillance sensitivity analysed using AFP surveillance criteria recommended by WHO and variable used in AFP surveillance system.

Results: Surveillance sensitivity is analysed based on two indicators "non polio AFP rate" and stool adequacy. Sensitivity level analysed in AFP cases aged 6-59 months for ≥7 OPV doses including routine and SIAs revealed 6/10 districts have high sensitivity.

Conclusion: Long absence of Polio virus in the area, creeping up of boredom among health human resource, Clinician's failure to notify all AFP cases resulting in down going Surveillance sensitivity.

Key Words: AFP, Polio eradication, Surveillance sensitivity

INTRODUCTION

PEI in Pakistan is haunted by campaign quality not improving; number of AFP cases /year declining, hope of identifying Polio virus transmission is not bright shrouded by the security challenges and political unrest. Precisely Pakistan is at high risk of missing target to interrupt Polio virus transmission by the end of 2014. In this study efforts are made to critically analyse the sensitivity of AFP surveillance system in AJK, as AJK is the only geographical area in Pakistan which has reported last case of WP (wild Poliovirus) in 2000 and maintained the status of interrupted wild polio virus circulation since then.

Aetiology of the Poliomyelitis was established nearly 109 years ago when Poliovirus was discovered during an experiment[1]. Experiments started about how the virus spreads in nervous system through blood and axonal transportation**.** 50 years later two vaccines were discovered to fight this crippling disease. Today Global Polio Eradication efforts succeed in containing Polio virus from 7 Continents to 3 countries, from 1000 cases per day to 1 case and from 3 strains to 1 strain today.

The emergency committee to monitor the Global Polio Eradication efforts met on 2014-05-28, 29 this year. Ten member states with ongoing Polio virus circulation participated in the meeting. Emergency committee affirmed that 60% of Wild Polio Virus circulation in seven countries (Cameroon, Equatorial Guinea, Ethiopia, Israel, Somalia and the Syrian Arab Republics) retransmitted through endemic countries (Pakistan, Nigeria and Afghanistan)[2] and there is dire need to declare Polio Eradication as IPHE (International Public Health Emergency).

By reviewing the current progress of the global initiative it seems the Pakistan will be the last country to eradicate Polio as Somalia was the last country to eliminate Small pox. 2014 emerged as a public health emergency as endemic countries failed to interrupt poliovirus transmission a GPEI target for 2010-2012[3]. Numbers of cases reported this year are higher than any of the time in past 5 years.

220 cases of WP1 reported in 2014 as compared to 64 last year by the end of 43 weeks, 29 districts found with ongoing Polio virus transmission as compared to 19 by the end 43 week in 2013. Environmental sampling results shows 87/263 (34%) sample positive for WP1 as compared to 47/265 (18%) positive for WP1 in 2013 by the end of 20 September[4]. At the moment Pakistan is the only state among endemic countries which has significant increase in number of WP1 cases reported through both AFP surveillance system and environmental sampling[5].

The impeded progress of Polio eradication in Pakistan is mainly because Polio is an enterovirus which has no extra human reservoir and infection commonly spread through oral-faecal route especially when hygiene and sanitation is poor[6]. Most of the people infected with

polio virus remain subclinical and very small proportion of infected people experience viral replication in CNS (central nervous system) which may lead to enduring neuronal damage and paralysis[7]. As we have discussed Polio case is most commonly recognized by onset of paralysis and paralysis occurs in 0.1% to 2% of Polio infected cases[8]. This elevated fraction of subclinical cases and no criteria to identify Polio by clinical signs and symptoms alone add to difficulty in eradicating Polio[9,10] and finally failure to reach to every eligible child during SIAs and routine EPI is the state specific issue for missing all the targets of Global Polio eradication in Pakistan. PEI in Pakistan is haunted by campaign quality not improving; number of AFP cases /year declining, hope of identifying Polio virus transmission is not bright shrouded by the security challenges and political unrest. Pakistan is specifically at high risk of missing target to interrupt Polio virus transmission by the end of 2014[11]. Number of cases reported in low transmission this year are very high for any of the low transmission season in last five years[12].

In this study efforts are made to critically analyse the sensitivity of AFP surveillance system in AJK, as AJK is the only geographical area in Pakistan which has reported last case of WP (wild Poliovirus) in 2000 and maintained the status of interrupted wild polio virus circulation since then.

District-Wise Area, Population, Density, Growth Rate & Household-Size in Azad Kashmir (Planning and development Department, 2012)

Districts	Area (Sq. KM)	Population Census 1998 (Million)		MICS 2007-2008	Projected Population in 2013 (million)	Density 2012 (Persons / Sq.KM
		Popu-lation	Growth rate	House-hold* Size		
Muzaffar-abad	1642	0.454	2.80%	5.8	0.695	407
Hattian	854	0.166	2.80%	5.8	0.254	286
Neelum	3621	0.126	2.80%	7.6	0.193	51
Mirpur	1010	0.333	2.09%	6.7	0.470	441
Bhimber	1516	0.302	2.60%	6.7	0.452	285
Kotli	1862	0.563	2.59%	7.3	0.841	432
Poonch	855	0.411	2.24%	6.8	0.589	655
Bagh	770	0.282	2.00%	6.8	0.393	483
Haveli	598	0.112	2.00%	6.8	0.156	246
Sudhnoti	569	0.224	1.99%	6.6	0.312	518
AJK	13297	2.973	2.41%	6.7	4.359	312

All the indicators were analysed based on WHO guidelines for successful AFP surveillance to eradicate Polio from Pakistan. WHO requires all the AFP cases age <15 years reported within 7 days of onset of paralysis, target for Pakistan is ≥2 cases / 100,000 children age <15 years. Two stool sample of each AFP cases taken 24 hours apart within 14 days of onset of paralysis, target is ≥80% adequate sample. Specimens arriving in national reference lab within ≥3 days of sent to lab in good conditions, target is ≥80%. Specimen with turnaround time ≥28days, turnaround time is time involving receipt of specimen and reporting of results, target is ≥80%. Stool specimen from which non polio enterovirus is isolated, target is ≥10% (this is the indicator of the quality of the reverse cold chain maintained during the collection and transportation of stool specimen).[13]

In the past AJK has maintained the campaigns quality and surveillance sensitivity to the level required for Polio eradication in the area. Population immunity against Polio remains the central subject for maintaining interrupted Polio virus circulation since 14 years. But risk of virus introduction has increased in the area because of decline in campaign and surveillance quality, IDPs coming to settle here from high risk areas, continuous mass movement towards and from the area of Polio virus circulation.

MATERIALS AND METHODS

Surveillance sensitivity analysed using AFP surveillance indicators for detecting poliovirus infection in children age <15 years in the study area based on few assumptions that all the results are negative and adequate information were available to make ultimate diagnosis of each AFP case reported in the area during study period.

Specificity of indicators is taken as WHO standard criteria for AFP surveillance according to which minimum rate of AFP case reporting is 2 cases/100,000 children < 15 years of age, 80% stool specimen collected within 14 days of onset of paralysis and stool testing considered to be the benchmark for excluding of poliovirus from AFP cases. Inadequate cases finally diagnosed by the ERC (Expert review committee) if residual weakness persists at 60 days follow up.

Each AFP case finally classified as Poliomyelitis if poliovirus isolated from stool sample, non polio AFP or compatible if system fails to collect stool sample within 14 days of onset of paralysis and sufficient proofs are not available to support the case as non polio AFP

Sensitivity evaluation conducted using AFP surveillance criteria recommended by WHO for AFP surveillance system. All the variables which describe surveillance arrangement and can manipulate the probability of disease or detecting the disease included in the analysis. Events that can bias the sampling methodology and size are included in the analysis. This research was recommended by the department of health AJK.

Districts: AJK government is responsible for providing curative and preventive health services in all districts through health department. Data analysed keeping in view the health services delivery structure in all the districts and surveillance sensitivity was analyzed at the districts level.

Age: Age was integrated to target the age specific categories of AFP cases, because the infection probability decreases with increase of age and vice versa apart from immunization status. But infection in >15 years age also depends on the severity of infection.

Population immunity; This risk category was integrated in the analysis as population immunity against Polio. OPV (oral polio vaccine) is the vaccine of choice used in both routine EPI (Expanded Program on Immunization) and SIAs (special Immunization activities).

In endemic countries most of the cases of poliomyelitis occurs in age <5 years (14)(8) and children play important role in the transmission of poliovirus infection. Population immunity is assessed by calculating OPV3 doses received by reported AFP cases through routine EPI aged 12-23 months and total OPV doses received through Routine EPI and SIAs doses aged 6-59 months.

RESULTS

Population immunity against Polio: District wise sensitivity level of Population immunity against polio and AFP Surveillance system to detect poliovirus if enter in the study area using surveillance data between 2001-2013. Data analysis revealed high sensitivity in all districts for routine EPI doses of OPV except moderate sensitivity in district Sudhnoti, Poonch and Neelum and district Neelum shows low sensitivity for routine EPI.

Sensitivity level analysed in AFP cases aged 6-59 months for ≥7 opv doses including routine and SIAs revealed 6/10 districts have high sensitivity. While districts 2/10 districts including Bhimber and Bagh fall in moderate and 2/10 districts including Poonch and Haveli falls in category of low sensitivity.

Surveillance sensitivity is analysed based on two indicators "non polio AFP rate" and stool adequacy. 5/10 districts have been placed in high sensitivity level for NPAFPR (non polio afp rate) while 3/10 districts in moderate sensitivity and 2/10 districts found having low sensitivity.

Sensitivity level for stool adequacy remains high 9/10 districts placed in high sensitivity level and only 1/10 district Haveli could only be placed in low sensitivity level.

Table No.1: Shows criteria for immunity & surveillance sensitivity analysis

Characteristics	high	Moderate	low
OPV3 dose age 12-24	≥95 %	80%-90%	<80%
≥7 SIAs OPV dose in age 6-59 m	≥90%	80%–90%	<80%
0 doses	<5%	5%–10%	>10%
Non-Polio AFP rate	≥2	1.5-2	<1.5
AFP cases with adequate specimen	≥80%	75%-80%	≤75%

Table No.2: Shows district wise sensitivity level of immunity and surveillance in AJK.

Districts	Sensitivity level of Immunity indicators			Sensitivity level of Surveillance indicators		Other risk levels	
	OPV3 Doses aged 12-24 m NPAFP	≥7D in age 6-59 m NPAFP	0 OPV doses in NPAFP	Non-Polio AFP rate	AFP cases with adequate specimen	Endemic Borders districts or Environmental sample +	Insecurity
Bhimber	High	Moderate	High	High	High	Yes	No
Bagh	High	Moderate	High	High	High	No	No
Kotli	High	High	High	Moderate	High	Yes	No
Sudnuti	Moderate	High	High	Moderate	High	Yes	No
Poonch	Moderate	Low	High	Moderate	High	Yes	No
Muzaffarabad	High	High	High	High	High	Yes	No
Hatyian	High	High	High	Low	High	No	No
Neelum	Moderate	High	High	High	High	No	No
Haveli	Low	Low	Low	Low	Low	No	No
Mirpur	High	High	High	High	High	Yes	No

DISCUSSION

Interruption of disease transmission is the decisive target of program now than ever because eradication is not possible without achieving this objective, mainly because high fraction of subclinical cases of Polio infection. Data analysis revealed that surveillance sensitivity in AJK vary from district to district and creeping down. Even if quality surveillance and population immunity against polio build accumulated surveillance sensitivity but several studies show several years without detection of case cannot assume low risk of reintroduction of poliovirus in the area.[15]

Persistent surveillance sensitivity is required to prevent poliovirus reintroduction in the area particularly when neighbouring areas are endemic and mass movement from and to the endemic areas exist on daily basis. Our study suggests that ≥95% confidence to keep the

poliovirus transmission interrupted in AJK at the prevalence of 10^{-5} need sustained sensitive AFP surveillance in the area. Achieving case notification 2 case/100,000 and stool adequacy ≥80% supported by the ≥95% coverage during SIAs and routine EPI is essential for eradicating Poliovirus.

Analysis of the historical data of the study area suggests long nonappearance of the poliovirus, stoppage of the clinicians to correlate non polio AFP cases with AFP surveillance system and presence of exact diagnosis resulting in decreased number of AFP cases in the area. Clinical decision making process of GPs (general practitioners) and child specialists further hampered the surveillance system. Environmental sampling can be proved as additional surveillance approach in AJK.

CONCLUSION

Long absence of Polio virus in the area, creep up of boredom among health human resource, Clinicians failure to notify all AFP cases resulting in downwards going Surveillance sensitivity. Findings of the study emphasize the AFP surveillance indicators up to required level of WHO to help eradicate Polio initiative globally and maintain poliovirus circulation interrupted in the study area. Beside Surveillance indicators up to the WHO standard needed for certification as a Polio free country.

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Original Article

HIV AIDS

Inter-Relationship of Viral Load and CD4+ Cells in Patients Suffering from Acquired Immuno Deficiency Syndrome (AIDS): Update from Punjab, Pakistan

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ABSTRACT

Objective: Purpose of current study was to evaluate the effect of antiretroviral drugs (Three regimen) Tenofovir, Lamivudine and Efavirenz to HIV patients presented in D.G. Khan Zone in regard to CD4 level and viral loads before start of drugs and after one year treatment.

Study Design: Comparative study

Place and Duration of Study: This study was carried out at the Institute of molecular biology and biotechnology (IMBB), and Centre for research in molecular medicine (CRiMM), The University of Lahore-Pakistan during May 2013 to Feb. 2014.

Materials and methods: Seventy five (75) patients suffering from HIV and twelve (12) control individuals were selected for the study from Dera Ghazi Khan during 2013-2014. Rapid testing and ELISA screening were performed for identification of presence/absence of virus and antibodies respectively. Viral load and CD4+ absolute count were also evaluated by PCR and Multiset software respectively. All the analytical work was performed at the Institute of molecular biology and biotechnology (IMBB), and Centre for research in molecular medicine (CRiMM), The University of Lahore-Pakistan.

Results: Statistically highly significant difference (P= 0.00) was observed regarding viral load before and after the treatment in HIV patients receiving combination therapy, ART (antiretroviral therapy). The viral load in control and HIV patients before and after the treatment was (0.00, $3.22x10^4$) and (0.00, $1.61x10^2$) respectively. The CD4+ cells levels in control and HIV patients before and after the treatment was (330.67, 186.29) and (171.92, 372.64) respectively. Inverse correlation was also recorded between viral loads (After) and CD4+ levels (After), (Viral Load Vs CD4+, r=-.328**).

Conclusion: It is concluded that from one year antiviral therapy in AIDS patients the viral load decrease from $3.22x10^4$ to $1.61x10^2$ and CD4+ count increased from 186.29 to 372.64 with no significant complications hence improve the AIDS patients' lives and minimize the spread of infection.

Key Words: Antiretroviral drugs, ART, Tenofovir, Lamivudine, Efavirenz, ELISA, CD4+, PCR, viral load, HIV AIDS.

INTRODUCTION

HIV is one of the major health problems which infect about 40 million people worldwide including 2.3 million children. Highly active Antiretroviral Therapy has reduced morbidity and mortality in HIV infected adult and children. WHO (2009)[1] stated that antiretroviral drugs are those drugs that are used for treatment and prevention of HIV infection. They work by stopping viral replication. There are different classes of antiretroviral drugs; Nucleoside reverse transcriptase inhibitors, Non nucleoside reverse transcriptase inhibitors, protein inhibitors and some other drugs are also available that inhibit viral process to make copies of itself. Paul and Deeks (2010)[2] stated that there are seventeen drugs that are used for treatment against HIV. They stated that anti retroviral therapy has changed HIV from fatal disease into chronic illness. They concluded that although complete cure against HIV is not possible but continued and combination ART therapy has increased life ling suppression of HIV replication. Despite of all this some limitations are still there and treatment success needs long time drug adherence.

MATERIALS AND METHODS

Patients form both genders, ages groups include children up to 60 years of age. The study was conducted from May 2013 to Feb. 2014. Seventy five (75) patients suffering from HIV and thirteen (13) control individuals were selected for the study from Dera Ghazi Khan. All the analytical work was

performed at the Institute of molecular biology and biotechnology (IMBB), and Centre for research in molecular medicine (CRiMM), The University of Lahore-Pakistan.

Following criteria was adopted to start anti-retro viral therapy.

1. Patient was a confirmed case of HIV/AIDS by rapid testing, by ELISA screening of detection of anti bodies and viral load by PCR.
2. CD4 absolute count. CD4 absolute count should be less than 350 cells/micro ml (normal range 450-1100)
3. Clinical Staging of the patients was determined.
4. Incidence of repeated opportunistic infection along with repeated Diarrhea.

Exclusion criteria:

1. Age above 70 years
2. CD4 absolute count more than 350 cells/micro ml.
3. Patient not willing to start antiretroviral therapy.

Methodology:

Rapid testing: 3CC of venous blood was taken and centrifuged, serum was separated and put on rapid kit along with buffer if 2 lines are appearing patient was positive. In case of negative only control line appeared on device. The first line was for control and second line was for patient (test).

ELISA Screening: Antibodies were detected by sandwich method of labeled prefilled antigen-antibody mixture and were compared with cut off ratio and determined the reactivity.

Viral Load by PCR: PCR facility was provided by Centre for Research in Molecular Medicine (CRiMM) and Institute of Molecular Biology and Biotechnology (IMBB), the University of Lahore, Lahore.

CD4 absolute Count: The absolute CD4 & CD8 count (absolute number of positive cellular events in sample compared to beads events) was determined by Multiset software and expressed in cells/ µl.

RESULTS

Data presented in Table-1 shows statistically highly significant difference (P=.000) was observed regarding viral load before and after the treatment in HIV patients receiving combination therapy, ART (Tenofovir-Lamivudine-Efavireinz). The viral load in control and HIV patients before and after the treatment was (0.00, $3.22x10^4$) and (0.00, 1.61 $x10^2$) respectively. The data regarding CD4+ cells depicted in table 01 also shows that with combination therapy, ART (Tenofovir-Lamivudine-Efavireinz), the levels of CD4+ cells was increased and a highly significant difference was recorded among control and ART treated patients. The CD4+ cells levels in control and HIV patients before and after the treatment was (330.67, 171.92) and (186.29, 372.64) respectively. Data in Table-2 (Pearson Correlation, Two Tailed**)** shows that a highly significant inverse relationship between viral load (Before) and CD4+ cell levels (Before) (Viral Load Vs CD4+, r = -.113**). Likewise inverse correlation was also recorded between viral loads (After) and CD4+ levels (After), (Viral Load Vs CD4+, r = -.328**).

Table No.1: Comparison of viral load and CD4+ among control and patients

	Group	n	Mean±SD	P value
Viral load (before)	Control	12	0.00±0.00	.000
	Patient	75	$3.22x10^4$±0.70	
Viral load (after)	Control	12	0.00±0.00	.000
	Patient	75	$1.61x10^2$±0.43	
CD4+ (before)	Control	12	330.67±77.07	.000
	Patient	75	186.29±29.02	
CD4+ (after)	Control	12	171.92±49.04	.000
	Patient	75	372.64±53.41	

Viral load: copies/mm CD4+: cells/mm^3

Table No.2: Pearson Correlation

	Viral load (before)	Viral load (after)	CD4+ (before)	CD4+ (after)
Viral load (before)	1	.161	.113	.036
	.	.137	.299	.739
Viral load (after)		1	.502**	-.328**
		.	.000	.002
CD4+ (before)			1	-.159
			.	.141
CD4+ (after)				1

**. Correlation is significant at 0.01 level (2-tailed)

DISCUSSION

US department of Health and Human source (2012)[3], reported that there are six classes of antiretroviral drugs; NNRTIs, NRTIs, Protease Inhibitors, Fusion Inhibitors, CCRS Antagonistism and integrase inhibitors. Treatment of HIV with three or more drugs from two different classes at right time will lead to undetectable viral load within three to six months. They also stated that physician should consider following points before stating ART; viral load, HIV related illness, CD4 cell count, opportunistic infections and pregnancy. Kelley et al. (2009)[4] concluded that these days antiretroviral therapy is potent, convenient and very well tolerated. They stated that if treatment with ART is started before advance stage of disease, they reduce plasma HIV RNA concentration to undetectable level. Although immunological response varies in different patient, most that begin therapy before advanced immunodeficiency e.g. CD4 count below

200cell/ul, show robust and sustained CD4 T-cell count again.

Zolopa et al., (2009)[5] stated that HIV treatment should be started with CD4 cell count below 350cells/ul but patient suffering from other opportunistic infections or cancer treatment can be stated with CD4 count above 350cells/ul. Yeni et al., (2004)[6] stated that treatment of HIV with HAART should be started in all symptomatic patients and in asymptomatic patient with CD4 count less than 200cell/ul. In asymptomatic patients with CD4 count more than 200cells/ul decision to start ART be made with rate of decrease of CD4 cells. U.S department of Health and Human resource, (2012)[3], concluded in his study that progression rate are consistent in those patients starting High antiretroviral therapy at CD4 cell count below 200cell/ul and are inconsistent in patient with CD4 cell count above 350cell/ul. Johnson et al., (1999)[7], reported that lamivudine, common name 3TC, is very good rug against HIV. It is very rapidly absorbed up to >80% and distributed in different extra vascular compartments. The drug is 5-60% excreted in urine and its half life is about 3 hours. Lamivudine has very little interaction with other drugs.

HIV/AIDS Statistics and Epidemiology Section (2009)[8] stated that potency of ART suppressed viral load in 90% patients. Cao et al., (2013)[9] stated that treatment of HIV-1with tenofovir is related with renal impairment. They concluded that tenofovir is not metabolized by enzyme CYP450, so is not eliminated from kidneys. This leads to decrease in GFR and renal toxicity. Scherzer et al., (2012)[10] concluded that tenofovir treatment lead to increased risk of three kidney diseases; proteinuria, rapid decline in kidney functions and development of CKD and this risk is irreversible.

CONCLUSION

It is concluded that from one year antiviral therapy in AIDS patients the viral load decrease from $3.22x10^4$ to $1.61x10^2$ and CD4+ count increased from 186.29 to 372.64 with no significant complications hence improve the AIDS patients' lives and minimize the spread of infection.

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ABSTRACT

In Original Article, It should consist of the following seven subheadings: **Objective, Study Design, Place and Duration of study, Materials & Methods, Results, Conclusion & Key Words** and should not more than 250 Words.

The second part consists of Introduction, Materials and Methods, Results, Discussion, Conclusion and References

References should be entered in text Vancouver Style in ascending order and in shape of numbers & superscript (e.g. [1,2,3,4])

INTRODUCTION

The start of the introduction should be Relevant. Reasons and Importance of the study should be clear. Give only strictly pertinent References and do not include data or conclusions from the work being reported.

MATERIALS & METHODS

The Population taken for the study should be uniform and Sample selection criteria should be reliable. Inclusion & Exclusion criteria should be clearly specified.

RESULTS

Present yours results in a logical sequence in the Text, Tables, Illustrations, figures and Graphs.

DISCUSSION

Emphasize the new and important aspects of the study and conclusions that follow from them.

CONCLUSION

In this link write the goals of the study.

RECOMMENDATIONS

When appropriate, may be included.

ACKNOWLEDGMENTS

List of all contributors who do not meet the criteria for Authorship, such as a person who provided purely technical help, writing assistance or department chair who provided only general support. Financial & Material support should be acknowledged.

REFERENCES

It should be in the **Vancouver style**. References should be numbered in the order in which they are cited in the text. At the end of the article, the full list of references should give the names and initials of all the authors. **(if the authors are more than 6, then et al should be followed after the 6th name).** Vancouver Style should be used like' The healing of tissues by C02 laser. Br J Surg 1971;58:222-5.

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